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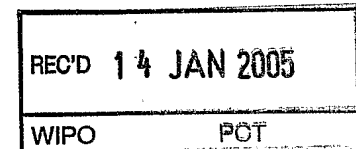
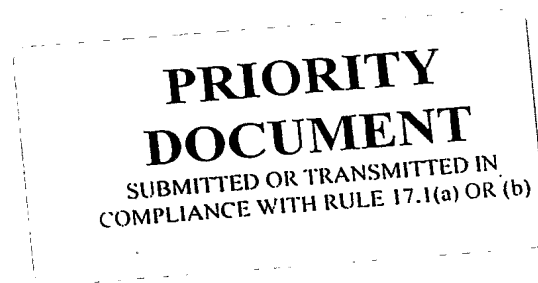
Die angehefteten Unterlagen stimmen mit der ursprünglich eingereichten Fassung der auf dem nächsten Blatt bezeichneten europäischen Patentanmeldung überein.

The attached documents are exact copies of the European patent application described on the following page, as originally filed.

Les documents fixés à cette attestation sont conformes à la version initialement déposée de la demande de brevet européen spécifiée à la page suivante.

Patentanmeldung Nr. Patent application No. Demande de brevet n°

03029844.2



Der Präsident des Europäischen Patentamts;  
Im Auftrag

For the President of the European Patent Office

Le Président de l'Office européen des brevets  
p.o.

R C van Dijk





PCT/EP 2004/017262

15.12.2004

Anmeldung Nr:  
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Anmelder/Applicant(s)/Demandeur(s):

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Bezeichnung der Erfindung/Title of the invention/Titre de l'invention:  
(Falls die Bezeichnung der Erfindung nicht angegeben ist, siehe Beschreibung.  
If no title is shown please refer to the description.  
Si aucun titre n'est indiqué se référer à la description.)

Plant growth regulation

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## Plant growth regulation

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Present invention relates to the technical field of agrochemicals and methods used in agriculture for plant growth regulation. In particular, the present invention relates to a new class of plant growth regulators for the treatment of plants in order to induce growth regulating responses which result in superior growth of treated plants, certain parts of the plants or, more generally, crop yield.

The term "method for plant growth regulation" or the term "growth regulation process" or the use of the words "plant growth regulation" or other terms using the word "regulate" as used in instant specification relate to a variety of plant responses which improve some characteristic of the plant. "Plant growth regulators" are compounds which possess activity in one or more growth regulation process(es) of a plant.

This type of plant growth regulation is distinguished from pesticidal action or growth reduction, sometimes also defined as a plant growth regulation, the intention of which, however, is to destroy or stunt the growth of a plant. For this reason, the compounds used in the practice of this invention are used in amounts which are non-phytotoxic with respect to the plant being treated but which stimulate the growth of the plant or certain parts thereof. Therefore, such compounds may also be called "plant stimulants", their action may be called as "plant growth stimulation".

25

Plant growth regulation is a desirable way to improve plants and their cropping so as to obtain improved plant growth and better conditions of agriculture practice compared to non-treated plants. This kind of molecules can either inhibit or promote cellular activities, often with a lower specificity compared to animal hormones. This means that plant growth regulators identified in plants most often regulate division, elongation and differentiation of plant cells in a way that, most often, they have multiple effects in plants.

30

On the molecular basis, plant growth regulators may work by affecting membrane properties, controlling gene expression or affecting enzyme activity or being active in a combination of at least two of the before mentioned types of interaction.

Plant growth regulators are chemicals either of natural origin, also called plant hormones (like non-peptide hormones e.g. auxins, giberrellins, cytokinins, ethylene, brassinosteroids or abscisic acid, and salicylic acid), lipooligosaccharides (e.g. Nod factors), peptides (e.g. systemin), fatty acid derivatives (e.g. jasmonates), and oligosaccharins (for review see: *Biochemistry & Molecular Biology of the Plant* (2000); eds. Buchanan, Gruissem, Jones, pp. 558-562; and 850-929), or they can be synthetically produced compounds (like derivatives of naturally occurring plant growth hormones, ethephon).

Plant growth regulators which work at very small concentrations can be found in many cells and tissues, but they seem to be concentrated in meristems and buds. Beside the selection of the right compound it is also relevant to look for the optimal environmental conditions because there are several factors known that may affect the action of growth hormones, like (a) the concentration of the plant growth regulator itself, (b) the quantity applied to the plant, (c) the time of application in relation to flowering date, (d) temperature and humidity prior to and after treatment, (e) plant moisture content; and several others.

Plant growth regulators can be either beneficial to the plant but sometimes can be used for weed control or to induce defoliation (like synthetic auxins 2,4-D and 2,4,5-T do).

The mode of action of existing plant growth regulators often is not known. Various targets are discussed and among those, most of the affected molecules are involved in cell division regulation, like arresting the cell cycle in stage G1 or G2, respectively, others for signaling drought stress responses (*Biochemistry & Molecular Biology of the Plant* (2000); eds. Buchanan, Gruissem, Jones, pp. 558-560). In any case, the hormone control can be identified as an extremely complex cascade of up and down regulations which, for example, can lead to a growth stimulation of one organ or cell typus of a plant but also can lead to a repression in other organs or cell typus of the same plant.

In many cases, kinases are involved either directly or indirectly in plant hormone control and among the kinases, protein kinases are central and highly specific control molecules in respect to cell cycle control. Such kinases are discussed as targets for several plant hormones, like it is the case for auxin and abscisic acid (Biochemistry & Molecular Biology of the Plant (2000); eds. Buchanan, Gruissem, Jones, pp. 542-565 and pp. 980-985; Morgan (1997), Annu. Rev. Cell. Dev. Biol., 13, 261-291; Amon et al. (1993), Cell, 74, pp. 993-1007; Dynlacht et al. (1997), Nature, 389, pp. 149-152; Hunt and Nasmyth (1997), Curr. Opin. Cell. Biol., 9, pp. 765-767; Thomas and Hall (1997), Curr. Opin. Cell Biol., 9, pp. 782-787).

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Cell cycle regulation plays a central role in animals as well (Cooper (2000), The Cell: A Molecular Approach, 2<sup>nd</sup> edition, Sinauer Associates Inc. ASM Press). It is known from WO 01/56567 that some 2,4-diamino-thiazole derivatives are inhibitors of specific protein kinases in mammals and may be used as pharmaceuticals for treatment of diseases in mammals, and especially in humans

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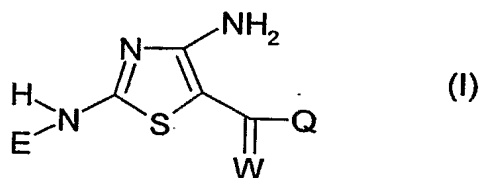
Among these protein kinases, GSK-3 is a protein-serine kinase involved in the hormonal control of several regulatory proteins, like via its ability to phosphorylate and inactivate glycogen synthase, which latter is the regulatory enzyme of glycogen synthesis in mammals (Embi et al. (1980), Eur. J. Biochem, 107, pp 519-527).

20

While WO01/56567 teaches that the 2,4-diaminothiazole derivatives are inhibitors of GSK 3, it does not teach or even suggest that plant growth can be regulated or stimulated or influenced in any other way by this class of compounds.

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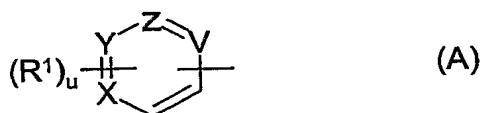
The present invention relates to the use of a compound for plant growth regulation, preferably by application of the compound to plants, to the seeds from which they grow or to the locus in which they grow, in an effective plant growth regulating, preferably non-phytotoxic amount, which compound is a 2,4-diamino-5-substituted-thiazole derivative of formula (I) or an agriculturally acceptable salt thereof:



wherein:

E is (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>3</sub>-C<sub>6</sub>)alkynyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy-(C<sub>1</sub>-C<sub>6</sub>)alkyl, [(C<sub>1</sub>-C<sub>6</sub>)alkoxy]carbonyl-(C<sub>1</sub>-C<sub>6</sub>)alkyl, [(C<sub>1</sub>-C<sub>6</sub>)alkyl]carbonyloxy-(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl-(C<sub>1</sub>-C<sub>6</sub>)alkyl, furfuryl, tetrahydrofurfuryl or isoxazolyl which last

- 5 mentioned group is unsubstituted or substituted with one or two (C<sub>1</sub>-C<sub>6</sub>)alkyl radicals; or is a group of formula (A):



- 10 in which X, Y, Z and V are each independently C or N, with the proviso that at least two of X, Y, Z and V are C;  
the linking bond of (A) is attached to a ring carbon atom;  
(R<sup>1</sup>)<sub>u</sub> are u substituents of R<sup>1</sup> which may be same or different, each R<sup>1</sup> is linked to a ring carbon atom and is H, R<sup>2</sup>, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl-(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl-(C<sub>1</sub>-C<sub>6</sub>)alkoxy, [(C<sub>3</sub>-C<sub>8</sub>)cycloalkyl]carbonyl, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyloxy, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl-S(O)<sub>m</sub>, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl or (C<sub>2</sub>-C<sub>6</sub>)alkynyl where each of the  
15 last 3 mentioned radicals is unsubstituted or substituted by one or more R<sup>2</sup> radicals; or aryl, heterocyclyl, aryl-(C<sub>1</sub>-C<sub>6</sub>)alkyl, heterocyclyl-(C<sub>1</sub>-C<sub>6</sub>)alkyl, aryl-(C<sub>1</sub>-C<sub>6</sub>)alkoxy, heterocyclyl-(C<sub>1</sub>-C<sub>6</sub>)alkoxy, aryl-carbonyl, heterocyclyl-carbonyl, aryloxy, heterocycliloxy, aryl-S(O)<sub>n</sub> or heterocyclyl-S(O)<sub>p</sub>, where the aryl or heterocyclyl  
20 portion of the last 12 mentioned radicals is unsubstituted or substituted by one to three radicals selected from the group consisting of R<sup>2</sup>, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl and (C<sub>2</sub>-C<sub>6</sub>)alkynyl, where each of the last 3 mentioned radicals is unsubstituted or substituted by one or two R<sup>2</sup> radicals;  
25 or (A) is fused to a 1,3-dioxolanyl or 1,4-dioxanyl ring where each of the last two mentioned rings is unsubstituted or substituted by one or more radicals selected from the group consisting of halogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy and OH;  
each R<sup>2</sup> independently from other R<sup>2</sup> radicals is hydroxy, halogen, cyano, nitro, NR<sup>3</sup>R<sup>4</sup>, CONR<sup>3</sup>R<sup>4</sup>, OCONR<sup>3</sup>R<sup>4</sup>, OCH<sub>2</sub>CONR<sup>3</sup>R<sup>4</sup>, (C<sub>1</sub>-C<sub>6</sub>)alkoxy, (C<sub>1</sub>-C<sub>6</sub>)haloalkoxy, CO<sub>2</sub>R<sup>3</sup>,  
30 COR<sup>3</sup>, NHCOR<sup>3</sup>, NHCO<sub>2</sub>R<sup>3</sup>, S(O)<sub>q</sub>R<sup>5</sup>, SO<sub>2</sub>NH<sub>2</sub> or R<sup>6</sup>;



- $R^3$  is hydrogen,  $(C_1-C_6)$ -alkyl or  $CH_2R^6$ ;  
 $R^4$  is hydrogen or  $(C_1-C_6)$ -alkyl; or  $R^3$  and  $R^4$  together with the nitrogen atom to which they are attached form a 3 to 8 membered cyclic ring optionally containing one or two further hetero atoms selected from oxygen, sulfur and nitrogen;
- 5  $R^5$  is  $(C_1-C_6)$ alkyl or  $(C_1-C_6)$ haloalkyl;  
 $W$  is O or N-OR<sup>7</sup>;  
 $R^6$  is phenyl unsubstituted or substituted by one or more radicals selected from the group consisting of halogen,  $(C_1-C_6)$ alkyl,  $(C_1-C_6)$ haloalkyl and  $(C_1-C_6)$ alkoxy;  
 $R^7$  is hydrogen,  $(C_1-C_6)$ alkyl or aryl- $(C_1-C_6)$ alkyl;
- 10  $Q$  is  $(C_3-C_8)$ cycloalkyl,  $(C_3-C_8)$ cycloalkyl- $(C_1-C_6)$ alkyl, where the last 2 mentioned radicals are unsubstituted or substituted in the cycloalkyl by  $(C_1-C_4)$ alkyl,  $(C_1-C_4)$ alkoxy and halogen,  $(C_1-C_6)$ alkyl,  $(C_2-C_6)$ alkenyl or  $(C_2-C_6)$ alkynyl, where each of the last 3 mentioned radicals is unsubstituted or substituted by one or two  $R^2$  radicals; or
- 15 aryl, heterocyclyl, aryl- $(C_1-C_6)$ alkyl or heterocyclyl- $(C_1-C_6)$ alkyl, where the aryl or heterocyclyl portion of the last 4 mentioned radicals is unsubstituted or substituted by:
- i) one to three radicals selected from the group consisting of  $R^2$ ,  $(C_1-C_6)$ alkyl,  $(C_2-C_6)$ alkenyl and  $(C_2-C_6)$ alkynyl, where each of the last 3 mentioned radicals is
- 20 unsubstituted or substituted by one or two  $R^2$  radicals; or
- ii)  $(C_3-C_8)$ cycloalkyl,  $(C_3-C_8)$ cycloalkyl- $(C_1-C_6)$ alkyl,  $(C_3-C_8)$ cycloalkyl- $(C_1-C_6)$ alkoxy,  $[(C_3-C_8)$ cycloalkyl]carbonyl,  $(C_3-C_8)$ cycloalkyloxy,  $(C_3-C_8)$ cycloalkyl-S(O)<sub>r</sub>, aryl, heterocyclyl, aryl- $(C_1-C_6)$ alkyl, heterocyclyl- $(C_1-C_6)$ alkyl, aryl- $(C_1-C_6)$ alkoxy, heterocyclyl- $(C_1-C_6)$ alkoxy, aryl-carbonyl, heterocyclyl-carbonyl, aryloxy,  $(C_3-C_8)$ -heterocycliloxy, aryl-S(O)<sub>s</sub> or heterocyclyl-S(O)<sub>t</sub>, which last 12 mentioned
- 25 radicals is unsubstituted or substituted by one or two radicals selected from the group consisting of  $(C_1-C_6)$ alkyl,  $(C_2-C_6)$ alkenyl,  $(C_2-C_6)$ alkynyl and  $R^2$ ;  
 $m$ ,  $n$ ,  $p$ ,  $q$ ,  $r$ ,  $s$  and  $t$  are each independently 0, 1 or 2;  
 $u$  is the number of ring carbon atoms in formula (A) minus 1;
- 30 and each heterocyclyl in the above-mentioned radicals is independently a heterocyclic radical having 3 to 7 ring atoms and 1, 2 or 3 hetero atoms in the ring selected from the group consisting of N, O and S.

These compounds possess valuable plant growth regulatory properties.

Formula (I) also encompasses any stereoisomer, enantiomer, geometric isomer or tautomer, and mixtures of the compounds of formula (I).

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By the term " agriculturally acceptable salts" is meant salts the anions or cations of which are known and accepted in the art for the formation of salts for agricultural use.

10 Suitable salts with bases, e.g. formed by compounds of formula (I) containing a carboxylic acid group, include alkali metal (e.g. sodium and potassium), alkaline earth metal (e.g. calcium and magnesium) and ammonium salts. The ammonium salts include ammonium ( $\text{NH}_4^+$ ) and ammonium salts of organic amines, (e.g. the diethanolamine, triethanolamine, octylamine, morpholine and dioctylmethylamine salts), and quaternary ammonium salts ( $\text{NR}_4^+$ ) for example tetramethylammonium.

15 Suitable acid addition salts, e.g. formed by compounds of formula (I) containing an amino group, include salts with inorganic acids, for example hydrochlorides, sulphates, phosphates and nitrates and salts with organic acids for example acetic acid.

20 It is to be understood that the  $\text{R}^1$  groups shown in formula (A) are attached only to ring carbon atoms.

In the present patent specification, including the accompanying claims, the aforementioned substituents have the following meanings:

25 Halogen means fluorine, chlorine, bromine or iodine.

The term "halo" before the name of a radical means that this radical is partially or completely halogenated, that is to say, substituted by F, Cl, Br, or I, in any combination.

30 The expression "( $\text{C}_1\text{-C}_6$ )alkyl" means an unbranched or branched non-cyclic saturated hydrocarbon radical having 1, 2, 3, 4, 5 or 6 carbon atoms (indicated by a range of C-atoms in the parenthesis), such as, for example a methyl, ethyl, propyl,

isopropyl, 1-butyl, 2-butyl, 2-methylpropyl or tert-butyl radical. The same applies to alkyl groups in composite radicals such as "alkoxyalkyl".

Alkyl radicals and also in composite groups, unless otherwise defined, preferably have 1 to 4 carbon atoms.

- 5    "(C<sub>1</sub>-C<sub>6</sub>)Haloalkyl" means an alkyl group mentioned under the expression "(C<sub>1</sub>-C<sub>6</sub>)alkyl" in which one or more hydrogen atoms are replaced by the same number of identical or different halogen atoms, such as monohaloalkyl, perhaloalkyl, CF<sub>3</sub>, CHF<sub>2</sub>, CH<sub>2</sub>F, CHFCH<sub>3</sub>, CF<sub>3</sub>CH<sub>2</sub>, CF<sub>3</sub>CF<sub>2</sub>, CHF<sub>2</sub>CF<sub>2</sub>, CH<sub>2</sub>FCHCl, CH<sub>2</sub>Cl, CCl<sub>3</sub>, CHCl<sub>2</sub> or CH<sub>2</sub>CH<sub>2</sub>Cl.
- 10   "(C<sub>1</sub>-C<sub>6</sub>)Alkoxy-(C<sub>1</sub>-C<sub>6</sub>)alkyl" means (C<sub>1</sub>-C<sub>6</sub>)alkyl which is substituted by (C<sub>1</sub>-C<sub>6</sub>)alkoxy.  
      "(C<sub>1</sub>-C<sub>6</sub>)Alkyl-S(O)<sub>n</sub>" means (C<sub>1</sub>-C<sub>6</sub>)alkylthio, alkylsulfinyl or alkylsulfonyl group, for example methylthio, methylsulfinyl or methylsulfonyl.  
      "(C<sub>1</sub>-C<sub>6</sub>)Alkylcarbonyl" means a (C<sub>1</sub>-C<sub>6</sub>)alkyl group which is attached to a carbonyl
- 15   group.  
      "(C<sub>1</sub>-C<sub>6</sub>)Alkoxy" means an alkoxy group whose carbon chain has the meaning given under the expression "(C<sub>1</sub>-C<sub>6</sub>)alkyl". "Haloalkoxy" is, for example, OCF<sub>3</sub>, OCHF<sub>2</sub>,  
20   OCH<sub>2</sub>F, CF<sub>3</sub>CF<sub>2</sub>O, OCH<sub>2</sub>CF<sub>3</sub> or OCH<sub>2</sub>CH<sub>2</sub>Cl.  
      "[(C<sub>1</sub>-C<sub>6</sub>)Alkoxy]carbonyl-(C<sub>1</sub>-C<sub>6</sub>)alkyl" means (C<sub>1</sub>-C<sub>6</sub>)alkyl which is substituted by a [(C<sub>1</sub>-C<sub>6</sub>)alkoxy]carbonyl group, for example ethoxycarbonylmethyl.  
      "(C<sub>2</sub>-C<sub>6</sub>)Alkenyl" means an unbranched or branched non-cyclic carbon chain having a number of carbon atoms which corresponds to this stated range and which
- 25   contains at least one double bond which can be located in any position of the respective unsaturated radical. "(C<sub>2</sub>-C<sub>6</sub>)Alkenyl" accordingly denotes, for example, the vinyl, allyl, 2-methyl-2-propenyl, 2-butenyl, pentenyl, 2-methylpentenyl or the hexenyl group.  
      "(C<sub>2</sub>-C<sub>6</sub>)Alkynyl" means an unbranched or branched non-cyclic carbon chain having
- 30   a number of carbon atoms which corresponds to this stated range and which contains one triple bond which can be located in any position of the respective

unsaturated radical. "(C<sub>2</sub>-C<sub>6</sub>)Alkynyl" accordingly denotes, for example, the propargyl, 1-methyl-2-propynyl, 2-butyne or 3-butyne group.

"(C<sub>3</sub>-C<sub>6</sub>)Cycloalkyl" denotes monocyclic alkyl radicals, such as the cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl radical. Cycloalkyl groups preferably have from

5 three to seven carbon atoms in the ring.

"(C<sub>3</sub>-C<sub>8</sub>)Cycloalkyl-(C<sub>1</sub>-C<sub>6</sub>)alkyl" means (C<sub>1</sub>-C<sub>6</sub>)alkyl which is substituted by (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl.

"(C<sub>3</sub>-C<sub>8</sub>)Cycloalkyloxy" means a (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl group which is attached to an O atom, for example cyclopropyloxy or cyclohexyloxy.

10 The term "aryl" means a carbocyclic aromatic ring system such as phenyl, biphenyl, naphthyl, anthracenyl, phenanthrenyl, fluorenyl, indenyl, pentalenyl, azulenyl, biphenylenyl and the like. Aryl is also intended to include the partially hydrogenated derivatives of the carbocyclic aromatic systems enumerated above, which contain at least one aromatic carbocyclic ring. Non-limiting examples of such partially

15 hydrogenated derivatives are 1, 2, 3, 4-tetrahydronaphthyl, 1, 4-dihydronaphthyl and the like.

A "heterocyclyl" group can be saturated, unsaturated or heteroaromatic; it preferably contains one or more, in particular 1, 2 or 3, hetero atoms in the heterocyclic ring, preferably selected from the group consisting of N, O and S; it is preferably an

20 aliphatic heterocyclyl radical having 3 to 7 ring atoms or a heteroaromatic radical having 5 to 7 ring atoms. The heterocyclic radical can be, for example, a

heteroaromatic radical or ring (heteroaryl) such as, for example, a mono-, bi- or polycyclic aromatic system in which at least 1 ring contains one or more hetero atoms, for example pyridyl, pyrimidinyl, pyridazinyl, pyrazinyl, triazinyl, thienyl, thiazolyl, thiadiazolyl, oxazolyl, isoxazolyl, furyl, pyrrolyl, pyrazolyl, imidazolyl and

25 triazolyl, or it is a partially or fully hydrogenated radical such as oxiranyl, oxetanyl, oxolanyl (= tetrahydrofuryl), oxanyl, pyrrolidyl, piperidyl, piperazinyl, dioxolanyl, oxazolyl, isoxazolyl, oxazolidinyl, isoxazolidinyl and morpholinyl. The

30 "heterocyclyl" group may be unsubstituted or substituted, preferably by one or more radicals (preferably 1, 2 or 3 radicals) selected from the group consisting of halogen, alkoxy, haloalkoxy, alkylthio, hydroxyl, amino, nitro, carboxyl, cyano, alkoxycarbonyl, alkylcarbonyl, formyl, carbamoyl, mono- and dialkylaminocarbonyl, substituted amino

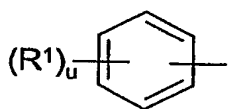
such as acylamino, mono- and dialkylamino, and alkylsulfinyl, haloalkylsulfinyl, alkylsulfonyl, haloalkylsulfonyl, alkyl and haloalkyl, and additionally also oxo. The oxo group can also be present at those hetero ring atoms where various oxidation numbers are possible, for example in the case of N and S.

- 5 "(C<sub>3</sub>-C<sub>8</sub>)-Heterocyclyloxy" means a heterocyclyl group which contains from 3 to 8 ring atoms which is attached to an oxygen atom.

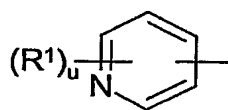
"Aryl-(C<sub>1</sub>-C<sub>6</sub>)alkyl", "heterocyclyl-(C<sub>1</sub>-C<sub>6</sub>)alkyl" and similar groups means (C<sub>1</sub>-C<sub>6</sub>)alkyl as defined above, substituted by aryl or heterocyclyl as defined above, for example benzyl or pyridylmethyl.

- 10 "Aryloxy" means an aryl group which is attached to an O atom, for example phenoxy. "Aryl-carbonyl" means an aryl group which is attached to a carbonyl group, for example benzoyl.

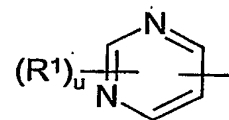
Preferably (A) is a formula (A1), (A2), (A3), (A4) or (A5):



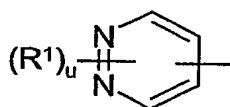
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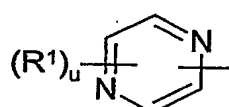
(A2)



(A3)



(A4)



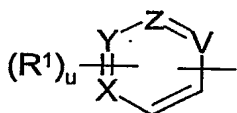
(A5)

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wherein R<sup>1</sup> and u are as defined above.

Preferably, E is (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy-(C<sub>1</sub>-C<sub>6</sub>)alkyl, [(C<sub>1</sub>-C<sub>6</sub>)alkoxy]carbonyl-(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl-(C<sub>1</sub>-C<sub>6</sub>)alkyl or a group (A):

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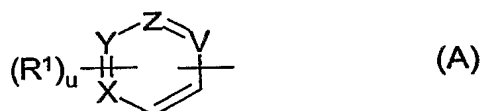
(A)

X, Y, Z and V are each C;

each  $R^1$  which may be the same or different is H, hydroxy, halogen, cyano, nitro,  $NR^3R^4$ ,  $CONR^3R^4$ ,  $(C_1-C_3)$ alkoxy,  $(C_1-C_3)$ haloalkoxy,  $CO_2R^3$ ,  $COR^3$ ,  $NHCOR^3$ ,  $S(O)_qR^5$ ,  $SO_2NH_2$ ,  $(C_1-C_3)$ alkyl or  $(C_1-C_3)$ haloalkyl, wherein  $R^3$  and  $R^4$  are each independently hydrogen or  $(C_1-C_3)$ -alkyl, and  $R^5$  is  $(C_1-C_3)$ alkyl or  $(C_1-C_3)$ haloalkyl;

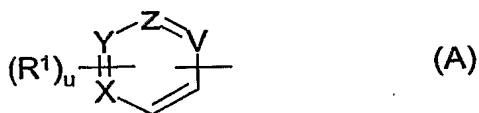
- 5 or phenyl or pyridyl, which last 2 mentioned radicals are unsubstituted or substituted by one to three radicals selected from the group consisting of halogen,  $(C_1-C_6)$ alkyl and  $(C_1-C_3)$ haloalkyl, and  $u$  is 5.

- 10 More preferably E is  $(C_1-C_3)$ alkyl,  $(C_1-C_3)$ alkoxy- $(C_1-C_3)$ alkyl,  $[(C_1-C_3)$ alkoxy]carbonyl- $(C_1-C_3)$ alkyl,  $(C_3-C_6)$ cycloalkyl- $(C_1-C_3)$ alkyl or a group of formula (A):



- 15 X, Y and Z are all C; V is C or N;  $R^1$  is H or halogen and  $u$  is 4 or 5.

Most preferably E is  $(C_1-C_3)$ alkyl,  $(C_1-C_3)$ alkoxy- $(C_1-C_3)$ alkyl,  $[(C_1-C_3)$ alkoxy]carbonyl- $(C_1-C_3)$ alkyl,  $(C_3-C_6)$ cycloalkyl- $(C_1-C_3)$ alkyl or a group (A):



20

X, Y, Z and V are all C;  $R^1$  is H or halogen; and  $u$  is 5.

Preferably W is O.

25

Preferably Q is  $(C_3-C_6)$ cycloalkyl,  $(C_3-C_6)$ cycloalkyl- $(C_1-C_3)$ alkyl,  $(C_1-C_3)$ alkyl,  $(C_1-C_3)$ haloalkyl,  $(C_3-C_4)$ alkenyl or  $(C_3-C_4)$ alkynyl; or

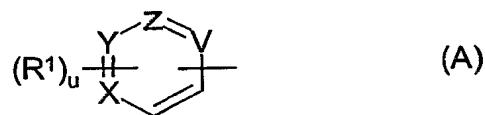
aryl, heterocyclyl, aryl-(C<sub>1</sub>-C<sub>6</sub>)alkyl or heterocyclyl-(C<sub>1</sub>-C<sub>6</sub>)alkyl, where the aryl or heterocyclyl portion of the last 4 mentioned radicals is unsubstituted or substituted by:

- 5 i) one to three radicals selected from the group consisting of hydroxy, halogen, cyano, nitro, NR<sup>3</sup>R<sup>4</sup>, CONR<sup>3</sup>R<sup>4</sup>, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, CO<sub>2</sub>R<sup>3</sup>, COR<sup>3</sup>, NHCOR<sup>3</sup>, S(O)<sub>q</sub>R<sup>5</sup>, SO<sub>2</sub>NH<sub>2</sub>, (C<sub>1</sub>-C<sub>6</sub>)alkyl and (C<sub>1</sub>-C<sub>3</sub>)haloalkyl; or
  - 10 ii) phenyl, heterocyclyl, benzyl, phenoxy or benzyloxy which last 5 mentioned radicals are unsubstituted or substituted by one or two radicals selected from the group consisting of (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, hydroxy, halogen, cyano, nitro, NR<sup>3</sup>R<sup>4</sup>, CONR<sup>3</sup>R<sup>4</sup>, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, CO<sub>2</sub>R<sup>3</sup>, COR<sup>3</sup>, NHCOR<sup>3</sup>, S(O)<sub>q</sub>R<sup>5</sup> and SO<sub>2</sub>NH<sub>2</sub>;
- R<sup>3</sup> and R<sup>4</sup> are each independently hydrogen or (C<sub>1</sub>-C<sub>3</sub>)-alkyl; and R<sup>5</sup> is (C<sub>1</sub>-C<sub>3</sub>)alkyl or (C<sub>1</sub>-C<sub>3</sub>)haloalkyl.
- 15 More preferably Q is (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, aryl or heteroaryl, which last 2 mentioned radicals are unsubstituted or substituted by one to three radicals selected from the group consisting of halogen, (C<sub>1</sub>-C<sub>3</sub>)alkyl, OH, NO<sub>2</sub>, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, phenyl and benzyloxy.
  - 20 Most preferably Q is cyclopropyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, phenyl, naphthyl, pyridinyl, tetrahydropyridinyl, thienyl or benzo[b]thienyl, which last 6 mentioned radicals are unsubstituted or substituted by one to three radicals selected from the group consisting of halogen, (C<sub>1</sub>-C<sub>3</sub>)alkyl, OH, NO<sub>2</sub>, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, phenyl and benzyloxy.

25

A preferred class of compounds of formula (I) for use in the invention are those in which:

E is (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy-(C<sub>1</sub>-C<sub>6</sub>)alkyl, [(C<sub>1</sub>-C<sub>6</sub>)alkoxy]carbonyl-(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl-(C<sub>1</sub>-C<sub>6</sub>)alkyl or a group (A):



wherein X, Y, Z and V are each C;

each  $R^1$  which may be the same or different is H, hydroxy, halogen, cyano, nitro,

5  $-NR^3R^4$ ,  $-CONR^3R^4$ ,  $(C_1-C_3)$ alkoxy,  $(C_1-C_3)$ haloalkoxy,  $CO_2R^3$ ,  $COR^3$ ,  $NHCOR^3$ ,

$S(O)_qR^6$ ,  $SO_2NH_2$ ,  $(C_1-C_3)$ alkyl or  $(C_1-C_3)$ haloalkyl, wherein  $R^3$  and  $R^4$  are each

independently hydrogen or  $(C_1-C_3)$ -alkyl, and  $R^5$  is  $(C_1-C_3)$ alkyl or  $(C_1-C_3)$ haloalkyl;

or phenyl or pyridyl, which last 2 mentioned radicals are unsubstituted or substituted

by one to three radicals selected from the group consisting of halogen,  $(C_1-C_6)$ alkyl

10 and  $(C_1-C_3)$ haloalkyl;

W is O;

Q is  $(C_3-C_6)$ cycloalkyl,  $(C_3-C_6)$ cycloalkyl- $(C_1-C_3)$ alkyl,  $(C_1-C_3)$ alkyl,  $(C_1-C_3)$ haloalkyl,

$(C_3-C_4)$ alkenyl or  $(C_3-C_4)$ alkynyl; or

aryl, heterocyclyl, aryl- $(C_1-C_6)$ alkyl or heterocyclyl- $(C_1-C_6)$ alkyl, where the aryl or

15 heterocyclyl portion of the last 4 mentioned radicals is unsubstituted or substituted by:

i) one to three radicals selected from the group consisting of hydroxy, halogen, cyano, nitro,  $-NR^3R^4$ ,  $-CONR^3R^4$ ,  $(C_1-C_3)$ alkoxy,  $(C_1-C_3)$ haloalkoxy,  $CO_2R^3$ ,  $COR^3$ ,  $NHCOR^3$ ,  $S(O)_qR^5$ ,  $SO_2NH_2$ ,  $(C_1-C_6)$ alkyl and  $(C_1-C_3)$ haloalkyl; or

20 ii) phenyl, heterocyclyl, benzyl, phenoxy or benzyloxy which last 5 mentioned radicals is unsubstituted or substituted by one or two radicals selected from the group consisting of  $(C_1-C_3)$ alkyl,  $(C_1-C_3)$ haloalkyl, hydroxy, halogen, cyano, nitro,  $NR^3R^4$ ,  $CONR^3R^4$ ,  $(C_1-C_3)$ alkoxy,  $(C_1-C_3)$ haloalkoxy,  $CO_2R^3$ ,  $COR^3$ ,  $NHCOR^3$ ,  $S(O)_qR^5$  and  $SO_2NH_2$ ;

25  $R^3$  and  $R^4$  are each independently hydrogen or  $(C_1-C_3)$ -alkyl, and  $R^5$  is  $(C_1-C_3)$ alkyl or  $(C_1-C_3)$ haloalkyl; and

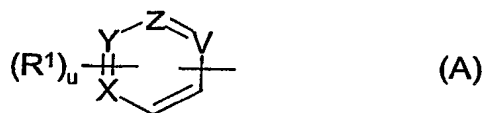
u is 5.

A more preferred class of compounds of formula (I) for use in the invention are those

30 in which:



E is (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy-(C<sub>1</sub>-C<sub>3</sub>)alkyl, [(C<sub>1</sub>-C<sub>3</sub>)alkoxy]carbonyl-(C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl-(C<sub>1</sub>-C<sub>3</sub>)alkyl or a group (A):



5

X, Y and Z are all C;

V is C or N;

R<sup>1</sup> is H or halogen;

W is O;

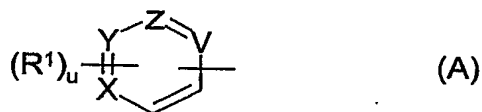
- 10 Q is (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, aryl or heteroaryl, which last 2 mentioned radicals are unsubstituted or substituted by one to three radicals selected from the group consisting of halogen, (C<sub>1</sub>-C<sub>3</sub>)alkyl, OH, NO<sub>2</sub>, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, phenyl and benzyloxy; and  
u is 4 or 5.

15

A most preferred class of compounds of formula (I) for use in the invention are those in which:

E is (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy-(C<sub>1</sub>-C<sub>3</sub>)alkyl, [(C<sub>1</sub>-C<sub>3</sub>)alkoxy]carbonyl-(C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl-(C<sub>1</sub>-C<sub>3</sub>)alkyl or a group (A):

20



X, Y, Z and V are all C;

W is O;

- 25 R<sup>1</sup> is H or halogen;

Q is cyclopropyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, phenyl, naphthyl, pyridinyl, tetrahydropyridinyl, thienyl or benzo[b]thienyl, which last 6 mentioned radicals are unsubstituted or substituted

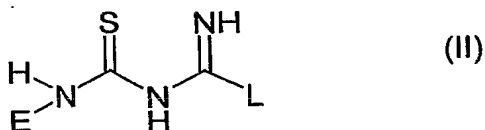
by one to three radicals selected from the group consisting of halogen, (C<sub>1</sub>-C<sub>3</sub>)alkyl, OH, NO<sub>2</sub>, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, phenyl and benzyloxy; and u is 5.

- 5 Compounds of formula (I) are partly known from WO 01/56567 and may be prepared according to WO 01/56567 and/or analogous to known methods (i.e. methods heretofore used or described in the literature).

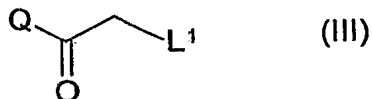
In the following description where symbols appearing in formulae are not specifically defined, it is to be understood that they are "as hereinbefore defined" in accordance with the first definition of each symbol in the specification.

10 It is to be understood that in the descriptions of the following processes, the sequences may be performed in different orders, and that suitable protecting groups may be required to achieve the compounds sought.

- 15 According to a feature of the invention compounds of formula (I) wherein E, and Q are as defined above and W is O, may be prepared by the reaction of a compound of formula (II):



- 20 wherein E is as defined above and L is a leaving group, with a compound of formula (III):



- wherein Q is as defined above and L<sup>1</sup> is a leaving group, for example chlorine or preferably bromine, in the presence of a base. A wide variety of leaving groups L
- 25 may be employed, and some preferred examples of these include N-bonded groups such as NH<sub>2</sub>, 1-pyrazolyl, 1,3-dimethylpyrazol-1-yl or 1,2,4-triazol-1-yl, or O or S bonded groups such as methoxy or thiomethoxy. Preferably a non-nucleophilic base is used, for example a trialkylamine such as triethylamine or pyridine. The reaction is preferably performed in the presence of a solvent such as N,N-dimethylformamide,

or a ketone such as acetone, or an alcohol such as ethanol, at a temperature of from 50°C to 150°C, more preferably from 80°C to 120°C.

The procedure is described for example by K.N.Rajasekharan in Synthesis, 5, 1986, pages 353-355.

5

According to a further feature of the invention compounds of formula (I) wherein E, and Q are as defined above and W is N-OR<sup>7</sup> wherein R<sup>7</sup> is as defined above, may be prepared by the reaction of the corresponding compound of formula (I) with a compound of formula (IV):

10



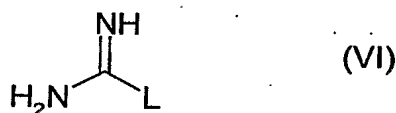
or a salt thereof, such as the hydrochloride or acetate salt. The reaction is generally performed in the presence of a base such as pyridine or a trialkylamine for example triethylamine, in a solvent such as tetrahydrofuran or dioxan, at a temperature of from 20°C to 100°C, preferably from 30°C to 70°C.

15

Compounds of formula (II) may be prepared by the reaction of a compound of formula (V):



20 wherein E is as defined above, with a compound of formula (VI):



or a salt thereof, wherein L is as defined above, in the presence of a base. The salts used are preferably those formed from a strong acid such as the nitrate or hydrohalide salt. A wide variety of bases may be used such as an alkali metal hydroxide or alkoxide for example sodium hydroxide or ethoxide, or an alkali metal carbonate or bicarbonate such as sodium carbonate or bicarbonate, or an organic base for example a trialkylamine such as triethylamine or pyridine. The amount of base used is generally more than 1 equivalent preferably from 1.1 to 1.5 equivalents. The reaction is generally performed in a solvent such as N,N-dimethylformamide, tetrahydrofuran or dioxan, at a temperature of from 0°C to 100°C, preferably from 20°C to 70°C. The compound of formula (II) is generally isolated, but may

25

30

alternatively be reacted in situ in a 1-pot process for the preparation of the compounds of formula (I).

5 Compounds of formula (III) are known or may be prepared according to known methods, for example as described in J. Organic. Chemistry, 29, 1964, pages 3459-3461. Compounds of formula (IV), (V) and (VI) are known or may be prepared according to known methods.

10 A collection of compounds of formula (I) which can be synthesized by the above-mentioned processes can additionally be prepared in parallel fashion, which can be effected manually, partly automated or fully automated. In this context, it is possible to automate the procedure of the reaction, work-up or purification of the products or intermediates. In total, this is to be understood as meaning a procedure which is described, for example, by S. H. DeWitt in "Annual Reports in Combinatorial  
15 Chemistry and Molecular Diversity: Automated Synthesis", Volume 1, published by Escom, 1997, pages 69 to 77.

For carrying out the reaction and work-up in parallel fashion, a series of commercially available apparatuses can be used as they are available from, for  
20 example, Stem Corporation, Woodrolfe Road, Tollesbury, Essex, CM9 8SE, England or Radleys Discovery Technologies, Saffron Walden, Essex, CB11 3AZ, England. To carry out the parallel purification of compounds (I) or of intermediates obtained during the preparation, there are available, inter alia, chromatographic equipment, for example from ISCO, Inc., 4700 Superior Street, Lincoln, NE 68504, USA. The  
25 equipment mentioned makes possible a modular procedure, where the individual steps are automated, but manual operation has to be carried out between the steps. This can be circumvented by employing partly or fully integrated automation systems, in which the automation modules in question are operated by, for example, robots. Such automation systems can be obtained from, for example, Zymark  
30 Corporation, Zymark Center, Hopkinton, MA 01748, USA.

In addition to the above-described methods, compounds of formula (I) can be prepared in full or partly by solid-phase supported methods. To this end, individual intermediates or all intermediates of the synthesis or of a synthesis adapted to the procedure in question are bound to a synthesis resin. Solid-phase supported synthetic methods are described extensively in the specialist literature, for example: Barry A. Bunin in "The Combinatorial Index", published by Academic Press, 1998. The use of solid-phase supported synthesis methods permits a series of protocols known from the literature which, in turn, can be carried out manually or in an automated fashion. For example, the "teabag method" (Houghten, US 4,631,211; Houghten et al., Proc. Natl. Acad. Sci., 1985, 82, 5131 – 5135) can be partly automated with products of IRORI, 11149 North Torrey Pines Road, La Jolla, CA 92037, USA. Solid-phase supported parallel synthesis can be automated successfully for example using equipment by Argonaut Technologies, Inc., 887 Industrial Road, San Carlos, CA 94070, USA or MultiSynTech GmbH, Wullener Feld 4, 58454 Witten, Germany.

The preparation in accordance with the processes described herein yields compounds of formula (I) in the form of substance collections or substance libraries. Subject matter of the present invention are therefore also libraries of the compounds of formula (I) which contain at least two compounds of formula (I), and of their precursors.

The following non-limiting Examples illustrate the preparation of the compounds of formula (I).

25

#### A. Chemical Examples

In the Examples which follow, quantities (also percentages) are weight based unless stated otherwise.

30

## Example 1

[4-Amino-2-(pyridin-3-yl-amino)-thiazol-5-yl]-(4-difluoromethoxyphenyl)-methanone  
(Compound 1.60)

- 5 A mixture 1-[(3,5-dimethylpyrazol-1-yl)-iminomethyl]-3-pyridin-3-yl-thiourea (170 mg, 0.62 mmol), 4-difluoromethoxy- $\alpha$ -bromoacetophenone (160 mg, 6.2 mmol) and triethylamine (100  $\mu$ l, 0.72 mmol) in N,N-dimethylformamide (2 ml) was heated at 60°C for 4 hours. Subsequently, an aqueous solution of ammonia (33%, 80 ml) was added and stirring was continued at 50 °C for 4 hours. After cooling to 20°C, the  
10 reaction mixture was diluted with water (1000 ml) and extracted with ethyl acetate (3x). The combined organic phase was dried over magnesium sulfate, filtered over silica and evaporated to dryness. The residue was triturated with chloroform to give the title compound (Compound 1.60, 126 mg, 56% yield) as a white crystals, mp 143 °C, <sup>1</sup>H NMR (DMSO-d<sub>6</sub>): 7.27 and 7.75 (AB-system, 4H), 7.36 (t, 1H), 7.40 (m, 1H),  
15 8.16 (m, 1H), 8.35 (m, 1H), 8.24 (bs, 2H), 8.83 (m, 1H), and 10.96 (bs, 1H).

The following Reference Example illustrates the preparation of intermediates used in the synthesis of the above Example.

## 20 Reference Example 1

1-[(3,5-Dimethyl-pyrazol-1-yl)-imino-methyl]-3-pyridin-3-yl-thiourea (Compound 2.8)

- To a stirred mixture of potassium hydroxide (85%, 4.50 g, 68.2 mmol) in N,N-dimethylformamide (70 ml) at 0 °C was added 3,5-dimethylpyrazole-carboxamidine  
25 nitrate (14.0, 68.2 mmol). The reaction mixture was allowed to warm up to 20°C, upon which the mixture became clear. Subsequently, 3-pyridylisothiocyanate (9.46 g, 68.0 mmol) was added and the reaction mixture was heated to 60 °C for 1 hour. After cooling to 20°C, ice-water was added (approx. 750 ml) and the resulting precipitate was collected by suction-filtration. The filter cake was washed with  
30 heptanes and triturated with water/ethanol (1:1) to yield give the title compound (13.1 g, 47.7 mmol, 70% yield) as pale yellow crystals, mp 132 °C.

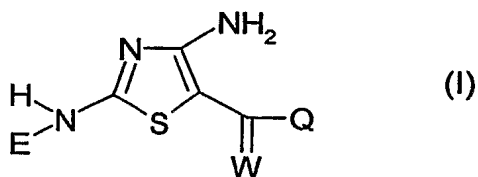
The following preferred compounds of formula (I) shown in Table 1 also form part of the present invention, and are obtained by, or analogously to, the above Example or the above-described general methods.

The following abbreviations are used in the Tables 1 and 2:

- 5 "Cpd" means Compound Number. Compound numbers are given for reference purposes only. In the Tables Ph means phenyl.

R<sub>f</sub> means retention time determined from thin layer chromatography on silica gel, using ethyl acetate as eluent.

- 10 Table 1: Compounds of formula (I) wherein W is O



Cpd	Q	E	mp (°C)	R <sub>f</sub>
1.1	C(CH <sub>3</sub> ) <sub>3</sub>	Ph	199	0.92
1.2	C(CH <sub>3</sub> ) <sub>3</sub>	4-OCH <sub>3</sub> -Ph		
1.3	C(CH <sub>3</sub> ) <sub>3</sub>	4-Cl-Ph		
1.4	C(CH <sub>3</sub> ) <sub>3</sub>	4-CN-Ph		
1.5	C(CH <sub>3</sub> ) <sub>3</sub>	4-CH <sub>3</sub> -Ph		
1.6	C(CH <sub>3</sub> ) <sub>3</sub>	3-CF <sub>3</sub> -Ph		
1.7	C(CH <sub>3</sub> ) <sub>3</sub>	4-CO <sub>2</sub> CH <sub>3</sub> -Ph		
1.8	C(CH <sub>3</sub> ) <sub>3</sub>	3-pyridyl		
1.9	C(CH <sub>3</sub> ) <sub>3</sub>	CH <sub>2</sub> -cyclohexyl		
1.10	C(CH <sub>3</sub> ) <sub>3</sub>	4-N(CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.11	C(CH <sub>3</sub> ) <sub>3</sub>	4-(OCH <sub>2</sub> Ph)-Ph		
1.12	C(CH <sub>3</sub> ) <sub>3</sub>	3-NO <sub>2</sub> -Ph		

Cpd	Q	E	mp (°C)	Rf
1.13	C(CH <sub>3</sub> ) <sub>3</sub>	4-SCH <sub>3</sub> -Ph		
1.14	C(CH <sub>3</sub> ) <sub>3</sub>	4-OCF <sub>3</sub> -Ph		
1.15	C(CH <sub>3</sub> ) <sub>3</sub>	5-F, 2-CH <sub>3</sub> -Ph		
1.16	C(CH <sub>3</sub> ) <sub>3</sub>	benzo[1,4]dioxin-6-yl		
1.17	C(CH <sub>3</sub> ) <sub>3</sub>	2-tetrahydrofurfuryl		
1.18	C(CH <sub>3</sub> ) <sub>3</sub>	2-furfuryl		
1.19	C(CH <sub>3</sub> ) <sub>3</sub>	5-methyl-isoxazol-3-yl		
1.20	C(CH <sub>3</sub> ) <sub>3</sub>	2-pyridyl		
1.21	C(CH <sub>3</sub> ) <sub>3</sub>	4-N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.22	C(CH <sub>3</sub> ) <sub>3</sub>	4-NHC(O)CH <sub>3</sub> -Ph		
1.23	C(CH <sub>3</sub> ) <sub>3</sub>	4-(1-piperidiny)-Ph		
1.24	C(CH <sub>3</sub> ) <sub>3</sub>	4-(4-Me-1-piperaziny)-Ph		
1.25	C(CH <sub>3</sub> ) <sub>3</sub>	4-(1-pyrroly)-Ph		
1.26	C(CH <sub>3</sub> ) <sub>3</sub>	4-(4-morpholiny)-Ph		
1.27	4-Cl-Ph	Ph	205	0.88
1.28	4-Cl-Ph	4-OCH <sub>3</sub> -Ph		
1.29	4-Cl-Ph	4-Cl-Ph		
1.30	4-Cl-Ph	4-CN-Ph		
1.31	4-Cl-Ph	4-CH <sub>3</sub> -Ph		
1.32	4-Cl-Ph	3-CF <sub>3</sub> -Ph		
1.33	4-Cl-Ph	4-CO <sub>2</sub> CH <sub>3</sub> -Ph		
1.34	4-Cl-Ph	3-pyridyl		
1.35	4-Cl-Ph	CH <sub>2</sub> -cyclohexyl		
1.36	4-Cl-Ph	4-N(CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.37	4-Cl-Ph	4-(OCH <sub>2</sub> Ph)-Ph		
1.38	4-Cl-Ph	3-NO <sub>2</sub> -Ph		



Cpd	Q	E	mp (°C)	Rf
1.39	4-Cl-Ph	4-SCH <sub>3</sub> -Ph		
1.40	4-Cl-Ph	4-OCF <sub>3</sub> -Ph		
1.41	4-Cl-Ph	5-F, 2-CH <sub>3</sub> -Ph		
1.42	4-Cl-Ph	benzo[1,4]dioxin-6-yl		
1.43	4-Cl-Ph	2-tetrahydrofurfuryl		
1.44	4-Cl-Ph	2-furfuryl		
1.45	4-Cl-Ph	5-methyl-isoxazol-3-yl		
1.46	4-Cl-Ph	2-pyridyl		
1.47	4-Cl-Ph	4-N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.48	4-Cl-Ph	4-NHC(O)CH <sub>3</sub> -Ph		
1.49	4-Cl-Ph	4-(1-piperidiny)-Ph		
1.50	4-Cl-Ph	4-(4-Me-1-piperaziny)-Ph		
1.51	4-Cl-Ph	4-(1-pyrroly)-Ph		
1.52	4-Cl-Ph	4-(4-morpholiny)-Ph		
1.53	4-OCHF <sub>2</sub> -Ph	Ph	195	0.88
1.54	4-OCHF <sub>2</sub> -Ph	4-OCH <sub>3</sub> -Ph	169	0.79
1.55	4-OCHF <sub>2</sub> -Ph	4-Cl-Ph	203	0.90
1.56	4-OCHF <sub>2</sub> -Ph	4-CN-Ph	250	0.92
1.57	4-OCHF <sub>2</sub> -Ph	4-CH <sub>3</sub> -Ph	184	0.87
1.58	4-OCHF <sub>2</sub> -Ph	3-CF <sub>3</sub> -Ph	222	0.93
1.59	4-OCHF <sub>2</sub> -Ph	4-CO <sub>2</sub> CH <sub>3</sub> -Ph	212	0.89
1.60	4-OCHF <sub>2</sub> -Ph	3-pyridyl	143	0.57
1.61	4-OCHF <sub>2</sub> -Ph	CH <sub>2</sub> -cyclohexyl	wax	0.82
1.62	4-OCHF <sub>2</sub> -Ph	4-N(CH <sub>3</sub> ) <sub>2</sub> -Ph	208	0.79
1.63	4-OCHF <sub>2</sub> -Ph	4-(OCH <sub>2</sub> Ph)-Ph		
1.64	4-OCHF <sub>2</sub> -Ph	3-NO <sub>2</sub> -Ph		

Cpd	Q	E	mp (°C)	Rf
1.65	4-OCHF <sub>2</sub> -Ph	4-SCH <sub>3</sub> -Ph		
1.66	4-OCHF <sub>2</sub> -Ph	4-OCF <sub>3</sub> -Ph		
1.67	4-OCHF <sub>2</sub> -Ph	5-F, 2-CH <sub>3</sub> -Ph		
1.68	4-OCHF <sub>2</sub> -Ph	benzo[1,4]dioxin-6-yl		
1.69	4-OCHF <sub>2</sub> -Ph	2-tetrahydrofurfuryl		
1.70	4-OCHF <sub>2</sub> -Ph	2-furfuryl		
1.71	4-OCHF <sub>2</sub> -Ph	5-methyl-isoxazol-3-yl		
1.72	4-OCHF <sub>2</sub> -Ph	2-pyridyl		
1.73	4-OCHF <sub>2</sub> -Ph	4-N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.74	4-OCHF <sub>2</sub> -Ph	4-NHC(O)CH <sub>3</sub> -Ph		
1.75	4-OCHF <sub>2</sub> -Ph	4-(1-piperidiny)-Ph		
1.76	4-OCHF <sub>2</sub> -Ph	4-(4-Me-1-piperaziny)-Ph		
1.77	4-OCHF <sub>2</sub> -Ph	4-(1-pyrrolyl)-Ph		
1.78	4-OCHF <sub>2</sub> -Ph	4-(4-morpholiny)-Ph		
1.79	2-thienyl	Ph	177	0.86
1.80	2-thienyl	4-OCH <sub>3</sub> -Ph	169	0.75
1.81	2-thienyl	4-Cl-Ph	202	0.85
1.82	2-thienyl	4-CN-Ph	292	0.86
1.83	2-thienyl	4-CH <sub>3</sub> -Ph	154	0.80
1.84	2-thienyl	3-CF <sub>3</sub> -Ph	229	0.90
1.85	2-thienyl	4-CO <sub>2</sub> CH <sub>3</sub> -Ph	227	0.81
1.86	2-thienyl	3-pyridyl	244	0.28
1.87	2-thienyl	CH <sub>2</sub> -cyclohexyl	198	0.68
1.88	2-thienyl	4-N(CH <sub>3</sub> ) <sub>2</sub> -Ph	234	0.62
1.89	2-thienyl	4-(OCH <sub>2</sub> C <sub>6</sub> H <sub>5</sub> )-Ph	184	0.76
1.90	2-thienyl	3-NO <sub>2</sub> -Ph	255	0.84

Cpd	Q	E	mp (°C)	Rf
1.91	2-thienyl	4-SCH <sub>3</sub> -Ph	196	0.79
1.92	2-thienyl	4-OCF <sub>3</sub> -Ph	225	0.86
1.93	2-thienyl	5-F, 2-CH <sub>3</sub> -Ph	210	0.81
1.94	2-thienyl	benzo[1,4]dioxin-6-yl	103	0.77
1.95	2-thienyl	2-tetrahydrofurfuryl		
1.96	2-thienyl	2-furfuryl		
1.97	2-thienyl	5-methyl-isoxazol-3-yl		
1.98	2-thienyl	2-pyridyl		
1.99	2-thienyl	4-N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.100	2-thienyl	4-NHC(O)CH <sub>3</sub> -Ph		
1.101	2-thienyl	4-(1-piperidiny)-Ph		
1.102	2-thienyl	4-(4-Me-1-piperaziny)-Ph		
1.103	2-thienyl	4-(1-pyrroly)-Ph		
1.104	2-thienyl	4-(4-morpholinyl)-Ph		
1.105	3-pyridyl	Ph	249	0.43
1.106	3-pyridyl	4-OCH <sub>3</sub> -Ph	224	0.35
1.107	3-pyridyl	4-Cl-Ph	242	0.42
1.108	3-pyridyl	4-CN-Ph	253	0.35
1.109	3-pyridyl	4-CH <sub>3</sub> -Ph	250	0.35
1.110	3-pyridyl	3-CF <sub>3</sub> -Ph	242	0.42
1.111	3-pyridyl	4-CO <sub>2</sub> CH <sub>3</sub> -Ph	237	0.35
1.112	3-pyridyl	3-pyridyl	178	0.07
1.113	3-pyridyl	CH <sub>2</sub> -cyclohexyl	153	0.28
1.114	3-pyridyl	4-N(CH <sub>3</sub> ) <sub>2</sub> -Ph	247	0.17
1.115	3-pyridyl	4-(OCH <sub>2</sub> Ph)-Ph	236	0.27
1.116	3-pyridyl	3-NO <sub>2</sub> -Ph	foam	0.23

Cpd	Q	E	mp (°C)	Rf
1.117	3-pyridyl	4-SCH <sub>3</sub> -Ph	220	0.26
1.118	3-pyridyl	4-OCF <sub>3</sub> -Ph	222	0.31
1.119	3-pyridyl	5-F, 2-CH <sub>3</sub> -Ph	214	0.30
1.120	3-pyridyl	benzo[1,4]dioxin-6-yl	205	0.23
1.121	3-pyridyl	2-tetrahydrofurfuryl		
1.122	3-pyridyl	2-furfuryl		
1.123	3-pyridyl	5-methyl-isoxazol-3-yl		
1.124	3-pyridyl	2-pyridyl		
1.125	3-pyridyl	4-N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.126	3-pyridyl	4-NHC(O)CH <sub>3</sub> -Ph		
1.127	3-pyridyl	4-(1-piperidiny)-Ph		
1.128	3-pyridyl	4-(4-Me-1-piperaziny)-Ph		
1.129	3-pyridyl	4-(1-pyrroly)-Ph		
1.130	3-pyridyl	4-(4-morpholiny)-Ph		
1.131	(a)	Ph		
1.132	(a)	4-OCH <sub>3</sub> -Ph		
1.133	(a)	4-Cl-Ph	wax	0.88
1.134	(a)	4-CN-Ph		
1.135	(a)	4-CH <sub>3</sub> -Ph		
1.136	(a)	3-CF <sub>3</sub> -Ph		
1.137	(a)	4-CO <sub>2</sub> CH <sub>3</sub> -Ph		
1.138	(a)	3-pyridyl		
1.139	(a)	CH <sub>2</sub> -cyclohexyl	foam	0.85
1.140	(a)	4-N(CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.141	(a)	4-(OCH <sub>2</sub> Ph)-Ph		
1.142	(a)	3-NO <sub>2</sub> -Ph		

Cpd	Q	E	mp (°C)	Rf
1.143	(a)	4-SCH <sub>3</sub> -Ph		
1.144	(a)	4-OCF <sub>3</sub> -Ph	wax	0.92
1.145	(a)	5-F, 2-CH <sub>3</sub> -Ph		
1.146	(a)	benzo[1,4]dioxin-6-yl		
1.147	(a)	2-tetrahydrofurfuryl		
1.148	(a)	2-furfuryl		
1.149	(a)	5-methyl-isoxazol-3-yl		
1.150	(a)	2-pyridyl		
1.151	(a)	4-N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.152	(a)	4-NHC(O)CH <sub>3</sub> -Ph		
1.153	(a)	4-(1-piperidiny)-Ph		
1.154	(a)	4-(4-Me-1-piperaziny)-Ph		
1.155	(a)	4-(1-pyrroly)-Ph		
1.156	(a)	4-(4-morpholin)-Ph		
1.157	cyclopropyl	Ph		
1.158	cyclopropyl	4-OCH <sub>3</sub> -Ph		
1.159	cyclopropyl	4-Cl-Ph		
1.160	cyclopropyl	4-CN-Ph		
1.161	cyclopropyl	4-CH <sub>3</sub> -Ph		
1.162	cyclopropyl	3-CF <sub>3</sub> -Ph		
1.163	cyclopropyl	4-CO <sub>2</sub> CH <sub>3</sub> -Ph		
1.164	cyclopropyl	3-pyridyl		
1.165	cyclopropyl	CH <sub>2</sub> -cyclohexyl		
1.166	cyclopropyl	4-N(CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.167	cyclopropyl	4-(OCH <sub>2</sub> Ph)-Ph		
1.168	cyclopropyl	3-NO <sub>2</sub> -Ph		

Cpd	Q	E	mp (°C)	Rf
1.169	cyclopropyl	4-SCH <sub>3</sub> -Ph		
1.170	cyclopropyl	4-OCF <sub>3</sub> -Ph		
1.171	cyclopropyl	5-F, 2-CH <sub>3</sub> -Ph		
1.172	cyclopropyl	benzo[1,4]dioxin-6-yl		
1.173	cyclopropyl	2-tetrahydrofurfuryl		
1.174	cyclopropyl	2-furfuryl		
1.175	cyclopropyl	5-methyl-isoxazol-3-yl		
1.176	cyclopropyl	2-pyridyl		
1.177	cyclopropyl	4-N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.178	cyclopropyl	4-NHC(O)CH <sub>3</sub> -Ph		
1.179	cyclopropyl	4-(1-piperidiny)-Ph		
1.180	cyclopropyl	4-(4-Me-1-piperazinyl)-Ph		
1.181	cyclopropyl	4-(1-pyrrolyl)-Ph		
1.182	cyclopropyl	4-(4-morpholinyl)-Ph		
1.183	4-OCF <sub>3</sub> -Ph	Ph		
1.184	4-OCF <sub>3</sub> -Ph	4-OCH <sub>3</sub> -Ph		
1.185	4-OCF <sub>3</sub> -Ph	4-Cl-Ph		
1.186	4-OCF <sub>3</sub> -Ph	4-CN-Ph		
1.187	4-OCF <sub>3</sub> -Ph	4-CH <sub>3</sub> -Ph		
1.188	4-OCF <sub>3</sub> -Ph	3-CF <sub>3</sub> -Ph		
1.189	4-OCF <sub>3</sub> -Ph	4-CO <sub>2</sub> CH <sub>3</sub> -Ph		
1.190	4-OCF <sub>3</sub> -Ph	3-pyridyl		
1.191	4-OCF <sub>3</sub> -Ph	CH <sub>2</sub> -cyclohexyl		
1.192	4-OCF <sub>3</sub> -Ph	4-N(CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.193	4-OCF <sub>3</sub> -Ph	4-(OCH <sub>2</sub> Ph)-Ph		
1.194	4-OCF <sub>3</sub> -Ph	3-NO <sub>2</sub> -Ph		

Cpd	Q	E	mp (°C)	Rf
1.195	4-OCF <sub>3</sub> -Ph	4-SCH <sub>3</sub> -Ph		
1.196	4-OCF <sub>3</sub> -Ph	4-OCF <sub>3</sub> -Ph		
1.197	4-OCF <sub>3</sub> -Ph	5-F, 2-CH <sub>3</sub> -Ph		
1.198	4-OCF <sub>3</sub> -Ph	benzo[1,4]dioxin-6-yl		
1.199	4-OCF <sub>3</sub> -Ph	2-tetrahydrofurfuryl		
1.200	4-OCF <sub>3</sub> -Ph	2-furfuryl		
1.201	4-OCF <sub>3</sub> -Ph	5-methyl-isoxazol-3-yl		
1.202	4-OCF <sub>3</sub> -Ph	2-pyridyl		
1.203	4-OCF <sub>3</sub> -Ph	4-N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.204	4-OCF <sub>3</sub> -Ph	4-NHC(O)CH <sub>3</sub> -Ph		
1.205	4-OCF <sub>3</sub> -Ph	4-(1-piperidiny)-Ph		
1.206	4-OCF <sub>3</sub> -Ph	4-(4-Me-1-piperaziny)-Ph		
1.207	4-OCF <sub>3</sub> -Ph	4-(1-pyrroly)-Ph		
1.208	4-OCF <sub>3</sub> -Ph	4-(4-morpholinyl)-Ph		
1.209	4-OCH <sub>3</sub> -Ph	Ph		
1.210	4-OCH <sub>3</sub> -Ph	4-OCH <sub>3</sub> -Ph		
1.211	4-OCH <sub>3</sub> -Ph	4-Cl-Ph		
1.212	4-OCH <sub>3</sub> -Ph	4-CN-Ph		
1.213	4-OCH <sub>3</sub> -Ph	4-CH <sub>3</sub> -Ph		
1.214	4-OCH <sub>3</sub> -Ph	3-CF <sub>3</sub> -Ph		
1.215	4-OCH <sub>3</sub> -Ph	4-CO <sub>2</sub> CH <sub>3</sub> -Ph		
1.216	4-OCH <sub>3</sub> -Ph	3-pyridyl		
1.217	4-OCH <sub>3</sub> -Ph	CH <sub>2</sub> -cyclohexyl		
1.218	4-OCH <sub>3</sub> -Ph	4-N(CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.219	4-OCH <sub>3</sub> -Ph	4-(OCH <sub>2</sub> Ph)-Ph		
1.220	4-OCH <sub>3</sub> -Ph	3-NO <sub>2</sub> -Ph		

Cpd	Q	E	mp (°C)	Rf
1.221	4-OCH <sub>3</sub> -Ph	4-SCH <sub>3</sub> -Ph		
1.222	4-OCH <sub>3</sub> -Ph	4-OCF <sub>3</sub> -Ph		
1.223	4-OCH <sub>3</sub> -Ph	5-F, 2-CH <sub>3</sub> -Ph		
1.224	4-OCH <sub>3</sub> -Ph	benzo[1,4]dioxin-6-yl		
1.225	4-OCH <sub>3</sub> -Ph	2-tetrahydrofurfuryl		
1.226	4-OCH <sub>3</sub> -Ph	2-furfuryl		
1.227	4-OCH <sub>3</sub> -Ph	5-methyl-isoxazol-3-yl		
1.228	4-OCH <sub>3</sub> -Ph	2-pyridyl		
1.229	4-OCH <sub>3</sub> -Ph	4-N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.230	4-OCH <sub>3</sub> -Ph	4-NHC(O)CH <sub>3</sub> -Ph		
1.231	4-OCH <sub>3</sub> -Ph	4-(1-piperidinyl)-Ph		
1.232	4-OCH <sub>3</sub> -Ph	4-(4-Me-1-piperazinyl)-Ph		
1.233	4-OCH <sub>3</sub> -Ph	4-(1-pyrrolyl)-Ph		
1.234	4-OCH <sub>3</sub> -Ph	4-(4-morpholinyl)-Ph		
1.235	4-CN-Ph	Ph		
1.236	4-CN-Ph	4-OCH <sub>3</sub> -Ph		
1.237	4-CN-Ph	4-Cl-Ph		
1.238	4-CN-Ph	4-CN-Ph		
1.239	4-CN-Ph	4-CH <sub>3</sub> -Ph		
1.240	4-CN-Ph	3-CF <sub>3</sub> -Ph		
1.241	4-CN-Ph	4-CO <sub>2</sub> CH <sub>3</sub> -Ph		
1.242	4-CN-Ph	3-pyridyl		
1.243	4-CN-Ph	CH <sub>2</sub> -cyclohexyl		
1.244	4-CN-Ph	4-N(CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.245	4-CN-Ph	4-(OCH <sub>2</sub> Ph)-Ph		
1.246	4-CN-Ph	3-NO <sub>2</sub> -Ph		



Cpd	Q	E	mp (°C)	Rf
1.247	4-CN-Ph	4-SCH <sub>3</sub> -Ph		
1.248	4-CN-Ph	4-OCF <sub>3</sub> -Ph		
1.249	4-CN-Ph	5-F, 2-CH <sub>3</sub> -Ph		
1.250	4-CN-Ph	benzo[1,4]dioxin-6-yl		
1.251	4-CN-Ph	2-tetrahydrofurfuryl		
1.252	4-CN-Ph	2-furfuryl		
1.253	4-CN-Ph	5-methyl-isoxazol-3-yl		
1.254	4-CN-Ph	2-pyridyl		
1.255	4-CN-Ph	4-N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.256	4-CN-Ph	4-NHC(O)CH <sub>3</sub> -Ph		
1.257	4-CN-Ph	4-(1-piperidiny)-Ph		
1.258	4-CN-Ph	4-(4-Me-1-piperaziny)-Ph		
1.259	4-CN-Ph	4-(1-pyrrolyl)-Ph		
1.260	4-CN-Ph	4-(4-morpholiny)-Ph		
1.261	1,3-benzodioxol-5-yl	Ph		
1.262	1,3-benzodioxol-5-yl	4-OCH <sub>3</sub> -Ph		
1.263	1,3-benzodioxol-5-yl	4-Cl-Ph		
1.264	1,3-benzodioxol-5-yl	4-CN-Ph		
1.265	1,3-benzodioxol-5-yl	4-CH <sub>3</sub> -Ph		
1.266	1,3-benzodioxol-5-yl	3-CF <sub>3</sub> -Ph		
1.267	1,3-benzodioxol-5-yl	4-CO <sub>2</sub> CH <sub>3</sub> -Ph		
1.268	1,3-benzodioxol-5-yl	3-pyridyl		
1.269	1,3-benzodioxol-5-yl	CH <sub>2</sub> -cyclohexyl		
1.270	1,3-benzodioxol-5-yl	4-N(CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.271	1,3-benzodioxol-5-yl	4-(OCH <sub>2</sub> Ph)-Ph		
1.272	1,3-benzodioxol-5-yl	3-NO <sub>2</sub> -Ph		

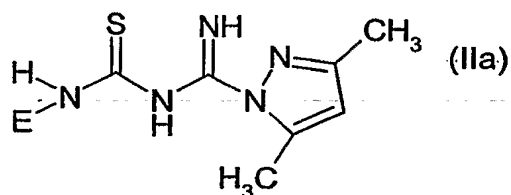
Cpd	Q	E	mp (°C)	Rf
1.273	1,3-benzodioxol-5-yl	4-SCH <sub>3</sub> -Ph		
1.274	1,3-benzodioxol-5-yl	4-OCF <sub>3</sub> -Ph		
1.275	1,3-benzodioxol-5-yl	5-F, 2-CH <sub>3</sub> -Ph		
1.276	1,3-benzodioxol-5-yl	benzo[1,4]dioxin-6-yl		
1.277	1,3-benzodioxol-5-yl	2-tetrahydrofurfuryl		
1.278	1,3-benzodioxol-5-yl	2-furfuryl		
1.279	1,3-benzodioxol-5-yl	5-methyl-isoxazol-3-yl		
1.280	1,3-benzodioxol-5-yl	2-pyridyl		
1.281	1,3-benzodioxol-5-yl	4-N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.282	1,3-benzodioxol-5-yl	4-NHC(O)CH <sub>3</sub> -Ph		
1.283	1,3-benzodioxol-5-yl	4-(1-piperidiny)-Ph		
1.284	1,3-benzodioxol-5-yl	4-(4-Me-1-piperaziny)-Ph		
1.285	1,3-benzodioxol-5-yl	4-(1-pyrrolyl)-Ph		
1.286	1,3-benzodioxol-5-yl	4-(4-morpholinyl)-Ph		
1.287	5-methoxy-thien-2-yl	Ph		
1.288	5-methoxy-thien-2-yl	4-OCH <sub>3</sub> -Ph		
1.289	5-methoxy-thien-2-yl	4-Cl-Ph		
1.290	5-methoxy-thien-2-yl	4-CN-Ph		
1.291	5-methoxy-thien-2-yl	4-CH <sub>3</sub> -Ph		
1.292	5-methoxy-thien-2-yl	3-CF <sub>3</sub> -Ph		
1.293	5-methoxy-thien-2-yl	4-CO <sub>2</sub> CH <sub>3</sub> -Ph		
1.294	5-methoxy-thien-2-yl	3-pyridyl		
1.295	5-methoxy-thien-2-yl	CH <sub>2</sub> -cyclohexyl		
1.296	5-methoxy-thien-2-yl	4-N(CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.297	5-methoxy-thien-2-yl	4-(OCH <sub>2</sub> Ph)-Ph		
1.298	5-methoxy-thien-2-yl	3-NO <sub>2</sub> -Ph		

Cpd	Q	E	mp (°C)	Rf
1.299	5-methoxy-thien-2-yl	4-SCH <sub>3</sub> -Ph		
1.300	5-methoxy-thien-2-yl	4-OCF <sub>3</sub> -Ph		
1.301	5-methoxy-thien-2-yl	5-F, 2-CH <sub>3</sub> -Ph		
1.302	5-methoxy-thien-2-yl	benzo[1,4]dioxin-6-yl		
1.303	5-methoxy-thien-2-yl	2-tetrahydrofurfuryl		
1.304	5-methoxy-thien-2-yl	2-furfuryl		
1.305	5-methoxy-thien-2-yl	5-methyl-isoxazol-3-yl		
1.306	5-methoxy-thien-2-yl	2-pyridyl		
1.307	5-methoxy-thien-2-yl	4-N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> -Ph		
1.308	5-methoxy-thien-2-yl	4-NHC(O)CH <sub>3</sub> -Ph		
1.309	5-methoxy-thien-2-yl	4-(1-piperidinyl)-Ph		
1.310	5-methoxy-thien-2-yl	4-(4-Me-1-piperazinyl)-Ph		
1.311	5-methoxy-thien-2-yl	4-(1-pyrrolyl)-Ph		
1.312	5-methoxy-thien-2-yl	4-(4-morpholinyl)-Ph		

Note: (a) is 1-(benzyloxycarbonylamino)-2-phenylethyl

Table 2: Reference Compounds of formula (IIa):

5



Cpd	E	mp (°C)	Rf
2.1	Ph	106	0.94
2.2	4-OCH <sub>3</sub> -Ph	129	0.87

Cpd	E	mp (°C)	Rf
2.3	4-Cl-Ph	120	0.90
2.4	4-CN-Ph	125	0.92
2.5	4-CH <sub>3</sub> -Ph	129	0.94
2.6	3-CF <sub>3</sub> -Ph	118	0.94
2.7	4-CO <sub>2</sub> CH <sub>3</sub> -Ph	159	0.90
2.8	3-pyridyl	132	0.70
2.9	CH <sub>2</sub> -cyclohexyl	89	0.95
2.10	4-N(CH <sub>3</sub> ) <sub>2</sub> -Ph	149	0.92
2.11	4-(OCH <sub>2</sub> Ph)-Ph	118	0.95
2.12	3-NO <sub>2</sub> -Ph	149	0.94
2.13	4-SCH <sub>3</sub> -Ph	117	0.93
2.14	4-OCF <sub>3</sub> -Ph	120	0.93
2.15	5-F, 2-CH <sub>3</sub> -Ph	122	0.94
2.16	2,3-dihydroxy-benzo[1,4]dioxin-6-yl	118	0.92
2.17	2-tetrahydrofurfuryl		
2.18	2-furfuryl		
2.19	5-methyl-isoxazol-3-yl		
2.20	2-pyridyl		
2.21	4-N(CH <sub>2</sub> CH <sub>3</sub> ) <sub>2</sub> -Ph		
2.22	4-NHC(O)CH <sub>3</sub> -Ph		
2.23	4-(1-piperidiny)-Ph		
2.24	4-(4-Me-1-piperazinyl)-Ph		
2.25	4-(1-pyrrolyl)-Ph		
2.26	4-(4-morpholinyl)-Ph		

- Another aspect of the invention is a method for plant growth regulation which plants are monocotyledoneous or dicotyledoneous crop plants, preferably selected from the group of economically important field crops such as, for example wheat, barley, rye, triticale, rice, maize, sugar beet, cotton, or soybeans, particularly maize, wheat, and soybean, as well as vegetables and ornamentals, said method comprising applying to said plants, to the seeds from which they grow or to the locus in which they grow, a non-phytotoxic, effective plant growth regulating amount of one or more compounds of formula (I).
- 10 A further aspect of the invention is a method for plant growth regulation, which plants are monocotyledoneous or dicotyledoneous crop plants, preferably selected from the group of economically important field crops such as, for example wheat, barley, rye, triticale, rice, maize, sugar beet, cotton, or soybeans, particularly maize, wheat, and soybean, as well as vegetables and ornamentals, said method comprising applying to said plants, to the seeds from which they grow or to the locus in which they grow, a non-phytotoxic, effective plant growth regulating amount of a compound having the formula (I) in a mixture with carriers and/or surfactants.
- 20 A further aspect of the invention is a method for plant growth regulation, which plants are monocotyledoneous or dicotyledoneous crop plants, preferably selected from the group of economically important field crops such as, for example wheat, barley, rye, triticale, rice, maize, sugar beet, cotton, or soybeans, particularly maize, wheat, and soybean, as well as vegetables and ornamentals, said method comprising applying to said plants, to the seeds from which they grow or to the locus in which they grow, a non-phytotoxic, effective plant growth regulating amount of a compound having the formula (I) together with a further active compound selected from the group consisting of acaricides, fungicides, herbicides, insecticides, nematocides or plant growth regulating substances not identical to compounds defined by formula (I).
- 30 Another aspect of the invention is a method for growth regulation in plant tissue cultures of monocotyledoneous or dicotyledoneous plants said method comprising applying to plant tissue cultures an appropriate amount of a compound having the

formula (I) either alone or together with at least one further active compound selected from the group of plant growth regulators or plant hormones.

The compounds of formula (I) can preferably be employed as plant growth regulators in crops of useful monocotyledoneous or dicotyledoneous crop plants, preferably selected from the group of economically important field crops such as, for example wheat, barley, rye, triticale, rice, maize, sugar beet, cotton, or soybeans, particularly maize, wheat, and soybeans, as well as vegetables and ornamentals, that have been rendered thus by means of genetic engineering.

Traditional ways of generating novel plants which have modified characteristics in comparison with existing plants consist, for example, in traditional breeding methods and the generation of mutants. However, it is also possible to generate novel plants with altered characteristics with the aid of genetic engineering methods (see, for example, EP-A-0221044, EP-A-0131624). For example, several cases have been described of

- genetic engineering modifications of crop plants with the purpose of modifying the starch synthesized in the plants (for example WO 92/11376, WO 92/14827, WO 91/19806),
- transgenic crop plants which are resistant to certain herbicides of the glufosinate type (cf., for example, EP-A-0242236, EP-A-242246) or the glyphosate type (WO 92/00377) or the sulfonylurea type (EP-A-0257993, US-A-5013659),
- transgenic crop plants, for example cotton, which are capable of producing *Bacillus thuringiensis* toxins (Bt toxins) which make the plants resistant to specific pests (EP-A-0142924, EP-A-0193259),
- transgenic crop plants whose fatty acid spectrum is modified (WO 91/13972).

A large number of techniques in molecular biology by means of which novel transgenic plants with altered characteristics can be generated are known in principle; see, for example, Sambrook et al., 1989, *Molecular Cloning, A Laboratory Manual*, 2nd Ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY; or

Winnacker "Gene und Klone" [Genes and Clones], VCH Weinheim 2nd Edition 1996, or Christou, "Trends in Plant Science" 1 (1996) 423-431).

5 In order to perform such genetic engineering manipulations, nucleic acid molecules may be introduced into plasmids which allow mutagenesis or a sequence change by means of recombination of DNA sequences. It is possible, for example, with the aid of the abovementioned standard methods to perform base exchanges, to remove subsequences or to add natural or synthetic sequences. To connect the DNA fragments to each other, adaptors or linkers may be attached to the fragments.

10

For example, plant cells with a reduced activity of a gene product can be generated by expressing at least one corresponding antisense RNA, a sense RNA to achieve a cosuppressory effect or by expressing at least one ribozyme of suitable construction which specifically cleaves transcripts of the abovementioned gene product.

15

To this end it is possible to make use of, on the one hand, DNA molecules which encompass the entire coding sequence of a gene product inclusive of any flanking sequences which may be present, on the other hand DNA molecules which only encompass parts of the coding sequence, but these parts must be long enough in order to effect, in the cells, an antisense effect. Use may also be made of DNA sequences which show a high degree of homology to the coding sequences of a gene product, but which are not completely identical.

20

When nucleic acid molecules are expressed in plants, the protein which has been synthesized may be located in any desired compartment of the plant cell. However, to achieve localization in a particular compartment, it is possible, for example, to link the coding region with DNA sequences which guarantee localization in a particular compartment. Such sequences are known to the skilled worker (see, for example, Braun et al., EMBO J. 11 (1992), 3219-3227; Wolter et al., Proc. Natl. Acad. Sci. USA 85 (1988), 846-850; Sonnewald et al., Plant J. 1 (1991), 95-106).

25

30

The transgenic plant cells may be regenerated by known techniques to give complete plants. In principle, the transgenic plants can be plants of any desired plant species, that is to say monocotyledonous and also dicotyledonous plants.

5 This allows transgenic plants to be obtained which exhibit altered characteristics by means of overexpression, suppression or inhibition of homologous (= natural) genes or gene sequences or by means of expression of heterologous (= foreign) genes or gene sequences.

10 The compounds of formula (I) can preferably be employed in transgenic crops which are resistant to herbicides from the group of the sulfonylureas, glufosinate-ammonium or glyphosate-isopropylammonium and analogous active substances or in analogous showing altered phenotypes, like but not limited to features as for content modification, altered flowering time, male or female sterile plants,  
15 environmentally resistant plants due to expression or repression of endogenous or exogenous genes in the transgenic crop.

The use according to the invention for plant growth regulation also includes the case where the compounds of formula (I) are only formed in the plant or the soil from a precursor ("prodrug") after its application to the plant.  
20

The compounds of formula (I) can be employed in the conventional preparations as wettable powders, emulsifiable concentrates, sprayable solutions, dusts or granules. The invention therefore also relates to plant growth regulating compositions which  
25 comprise compounds of formula (I).

According to a further feature of the present invention, there is provided a plant growth regulating composition comprising an effective amount of a compound of formula (I) as defined above or an agriculturally acceptable salt thereof, in  
30 association with, and preferably homogeneously dispersed in, one or more compatible agriculturally- acceptable diluents or carriers and/or surface active agents [i.e. diluents or carriers and/or surface active agents of the type generally accepted



in the art as being suitable for use in herbicidal compositions and which are compatible with compounds of the invention]. The term "homogeneously dispersed" is used to include compositions in which the compounds of formula (I) are dissolved in other components. The term "growth regulating composition" is used in a broad  
 5 sense to include not only compositions which are ready for use as herbicides but also concentrates which must be diluted before use (including tank mixtures).

The compounds of formula (I) can be formulated in various ways, depending on the prevailing biological and/or chemico-physical parameters. Examples of possible  
 10 formulations which are suitable are: wettable powders (WP), water-soluble powders (SP), water-soluble concentrates, emulsifiable concentrates (EC), emulsions (EW) such as oil-in-water and water-in-oil emulsions, sprayable solutions, suspension concentrates (SC), dispersions on an oil or water basis, solutions which are miscible with oil, capsule suspensions (CS), dusts (DP), seed-dressing products, granules for  
 15 broadcasting and soil application, granules (GR) in the form of microgranules, spray granules, coated granules and adsorption granules, water-dispersible granules (WG), water-soluble granules (SG), ULV formulations, microcapsules and waxes.

These individual formulation types are known in principle and described, for  
 20 example, in: Winnacker-Küchler, "Chemische Technologie" [Chemical Technology], Volume 7, C. Hauser Verlag, Munich, 4th Edition 1986; Wade van Valkenburg, "Pesticide Formulations", Marcel Dekker, N.Y., 1973; K. Martens, "Spray Drying Handbook", 3rd Ed. 1979, G. Goodwin Ltd. London.

25 The necessary formulation auxiliaries such as inert materials, surfactants, solvents and other additives are also known and described, for example, in: Watkins, "Handbook of Insecticide Dust Diluents and Carriers", 2nd Ed., Darland Books, Caldwell N.J.; H.v. Olphen, "Introduction to Clay Colloid Chemistry", 2nd Ed., J. Wiley & Sons, N.Y.; C. Marsden, "Solvents Guide", 2nd Ed., Interscience, N.Y. 1963;  
 30 McCutcheon's "Detergents and Emulsifiers Annual", MC Publ. Corp., Ridgewood N.J.; Sisley and Wood, "Encyclopedia of Surface Active Agents", Chem. Publ. Co. Inc., N.Y. 1964; Schönfeldt, "Grenzflächenaktive Äthylenoxidaddukte" [Surface-

active ethylene oxide adducts], Wiss. Verlagsgesell., Stuttgart 1976; Winnacker-Küchler, "Chemische Technologie" [Chemical Technology], Volume 7, C. Hauser Verlag, Munich, 4th Ed. 1986.

- 5    Based on these formulations, it is also possible to prepare combinations with pesticidally active substances such as, for example, insecticides, acaricides, herbicides, fungicides, and with safeners, fertilizers and/or growth regulators, for example in the form of a readymix or a tank mix.
- 10    Wettable powders are preparations which are uniformly dispersible in water and which, besides the compounds of formula (I), also comprise ionic and/or nonionic surfactants (wetters, dispersants), for example, polyoxyethylated alkylphenols, polyoxyethylated fatty alcohols, polyoxyethylated fatty amines, fatty alcohol polyglycol ether sulfates, alkanesulfonates or alkylbenzenesulfonates, sodium  
15    lignosulfonate, sodium 2,2'-dinaphthylmethane-6,6'-disulfonate, sodium dibutyl-naphthalenesulfonate or else sodium oleoylmethyltaurate, in addition to a diluent or inert substance. To prepare the wettable powders, the compounds of formula (I) are, for example, ground finely in conventional apparatuses such as hammer mills, blower mills and air-jet mills and mixed with the formulation auxiliaries,  
20    either concomitantly or thereafter.

- Emulsifiable concentrates are prepared, for example, by dissolving the compounds of formula (I) in an organic solvent, for example butanol, cyclohexanone, dimethylformamide, xylene or else higher-boiling aromatics or hydrocarbons or  
25    mixtures of these, with addition of one or more ionic and/or nonionic surfactants (emulsifiers). Emulsifiers which can be used are, for example: calcium salts of alkylarylsulfonic acids, such as calcium dodecylbenzenesulfonate or nonionic emulsifiers, such as fatty acid polyglycol esters, alkylaryl polyglycol ethers, fatty alcohol polyglycol ethers, propylene oxide/ethylene oxide condensates, alkyl  
30    polyethers, sorbitan esters such as sorbitan fatty acid esters or polyoxyethylene sorbitan esters such as polyoxyethylene sorbitan fatty acid esters.

Dusts are obtained by grinding the active substance with finely divided solid substances, for example talc or natural clays, such as kaolin, bentonite or pyrophyllite, or diatomaceous earth.

- 5    Suspension concentrates may be water- or oil-based. They can be prepared, for example, by wet grinding by means of commercially available bead mills, if appropriate with addition of surfactants, as they have already been mentioned above for example in the case of the other formulation types.
- 10   Emulsions, for example oil-in-water emulsions (EW), can be prepared for example by means of stirrers, colloid mills and/or static mixtures using aqueous organic solvents and, if appropriate, surfactants as they have already been mentioned above for example in the case of the other formulation types.
- 15   Granules can be prepared either by spraying the compounds of formula (I) onto adsorptive, granulated inert material or by applying active substance concentrates onto the surface of carriers such as sand, kaolinities or of granulated inert material, by means of binders, for example polyvinyl alcohol, sodium polyacrylate or alternatively mineral oils. Suitable active substances can also be granulated in the
- 20   manner which is conventional for the production of fertilizer granules, if desired in a mixture with fertilizers.

Water-dispersible granules are prepared, as a rule, by the customary processes such as spray-drying, fluidized-bed granulation, disk granulation, mixing in high-

25   speed mixers and extrusion without solid inert material. To prepare disk, fluidized-bed, extruder and spray granules, see, for example, processes in "Spray-Drying Handbook" 3rd ed. 1979, G. Goodwin Ltd., London; J.E. Browning, "Agglomeration", Chemical and Engineering 1967, pages 147 et seq.; "Perry's Chemical Engineer's Handbook", 5th Ed., McGraw-Hill, New York 1973, p. 8-57.

30

For further details on the formulation of crop protection products, see, for example, G.C. Klingman, "Weed Control as a Science", John Wiley and Sons, Inc., New York,

1961, pages 81-96 and J.D. Freyer, S.A. Evans, "Weed Control Handbook", 5th Ed., Blackwell Scientific Publications, Oxford, 1968, pages 101-103.

As a rule, the agrochemical preparations comprise 0.1 to 99% by weight, in particular

5 0.1 to 95% by weight, of compounds of formula (I).

The concentration of compounds of formula (I) in wettable powders is, for example, approximately 10 to 90% by weight, the remainder to 100% by weight being composed of customary formulation components. In the case of emulsifiable concentrates, the concentration of compounds of formula (I) can amount to

10 approximately 1 to 90, preferably 5 to 80% by weight. Formulations in the form of dusts usually comprise 1 to 30% by weight of compounds of formula (I), preferably in most cases 5 to 20% by weight of compounds of formula (I), while sprayable solutions comprise approximately 0.05 to 80, preferably 2 to 50% by weight of compounds of formula (I). In the case of water-dispersible granules, the content of

15 compounds of formula (I) depends partly on whether the compounds of formula (I) are in liquid or solid form and on which granulation auxiliaries, fillers and the like are being used. The water-dispersible granules, for example, comprise between 1 and 95% by weight of active substance, preferably between 10 and 80% by weight.

20 In addition, the formulations of compounds of formula (I) mentioned comprise, if appropriate, the adhesives, wetters, dispersants, emulsifiers, penetrants, preservatives, antifreeze agents, solvents, fillers, carriers, colorants, antifoams, evaporation inhibitors, pH regulators and viscosity regulators which are conventional in each case.

25

Suitable formulations for plant growth regulating compositions are known. A description of suitable formulations which may be used in the method of the invention can be found in international patent publications WO 87/3781, WO 93/6089, and WO 94/21606 as well as in European patent application EP 295117, and US Patent 5,232,940. Formulations or compositions for plant growth regulating

30 uses can be made in a similar way, adapting the ingredients, if necessary, to make them more suitable to the plant or soil to which the application is to be made.

The compounds of the formula (I) or their salts can be employed as such or in the form of their preparations (formulations) as combinations with other pesticidally active substances, such as, for example, insecticides, acaricides, nematocides,  
 5 herbicides, fungicides, safeners, fertilizers and/or further growth regulators, for example as a premix or as tank mixes.

It has been found that, surprisingly, the compounds of formula (I) and most especially compounds 1.1; 1.27; 1.53; 1.54; 1.55; 1.56; 1.57; 1.58; 1.59; 1.60; 1.61;  
 10 1.62; 1.81; 1.82; 1.83; 1.84; 1.85; 1.86; 1.87; 1.88; 1.89; 1.90; 1.91; 1.92; 1.93; 1.94; 1.105; 1.106; 1.107; 1.108; 1.109; 1.110; 1.111; 1.112; 1.113; 1.114; 1.115; 1.116; 1.117; 1.118; 1.119; 1.120; 1.133; 1.144; 2.1; 2.2; 2.3; 2.4; 2.5; 2.6; 2.7; 2.8; 2.9; 2.10; 2.11; 2.12; 2.13; 2.14; 2.15; and 2.16 display a significant role concerning plant growth properties, which can be different due to an application at various crops. For  
 15 example example, compounds 1.53; 1.58 show superior effects by being used as plant growth regulator in maize and wheat, but at different concentrations. Compounds 1.105; 1.106; 1.108 show at least a superior effect on wheat at various concentrations, whereas compounds 1.60; 1.79 show a superior effect concerning maize.

20

By virtue of the practice of the present invention a wide variety of plant growth responses, including the following (non-ranked listing), may be induced:

- a) more developed root system
- b) tillering increase
- 25 c) increase in plant height
- d) bigger leaf blade
- e) less dead basal leaves
- f) stronger tillers
- g) greener leaf color
- 30 h) less fertilizers needed
- i) less seeds needed
- j) more productive tillers

- k) less third non-productive tillers
- l) earlier flowering
- m) early grain maturity
- n) less plant verse (lodging)
- o) longer panicles
- p) increased shoot growth
- q) improved plant vigour
- r) early germination
- s) more fruit and better yield

10

It is intended that as used in the instant specification the term "method for plant growth regulation" or "method for plant growth regulation" means the achievement of any of the aforementioned nineteen categories of response or any other modification of plant, seed, fruit or vegetable (whether the fruit or vegetable is nor harvested or harvested) so long as the net result is to increase growth or benefit any property of the plant, seed, fruit or vegetable as distinguished from any pesticidal action (unless the present invention is practised in conjunction with or in the presence of a pesticide, for example a herbicide). The term "fruit" as used in the instant specification is to be understood as meaning anything of economic value that is produced by the plant.

20

Preferably, at least an increase of 10% of one or more of the respective plant growth response is obtained.

25

The 2,4-diamino-5-substituted-thiazole derivatives of formula (I) may be applied for plant growth regulating purposes to the foliage of plants and/or to the soil in which said plants are growing. Applications to the soil are often in the form of granules which are usually applied in sufficient amount to provide a rate of from about 0.001 kg/ha to about 0.5 kg/ha of active ingredient, preferably between 0.01 and 0.1 kg/ha.

30

A preferred embodiment of the invention is a method for plant growth regulation comprising applying to the seeds from which said plants grow, prior to said seeds, a non-phytotoxic, effective plant growth regulating amount of a compound having the

formula (I). The seed may be treated, especially by coating or embedding or impregnation or soaking or dipping in liquid or paste formulations which are known per se and are subsequently dried. Seed comprising 2 to 1000 gram per 100 kg of a compound of formula (I), preferably 5 to 800 g per 100 kg, most preferably 5 to 250 g per 100 kg are particularly appropriate for this purpose.

The precise amount of 2,4-diamino-5-substituted-thiazole derivatives compound to be used will depend, *inter alia*, upon the particular plant species being treated. A suitable dose may be determined by the man skilled in the art by routine experimentation. The plant response will depend upon the total amount of compound used, as well as the particular plant species which is being treated. Of course, the amount of 2,4-diamino-5-substituted-thiazole derivatives should be non-phytotoxic with respect to the plant being treated.

Although the preferred method of application of the compounds used in the process of this invention is directly to the foliage and stems of plants, the compounds can be applied to the soil in which the plants are growing.

The following examples are illustrative of methods of plant growth regulation according to the invention, but should not be understood as limiting the invention as modifications in materials and methods will be apparent to the skilled worker. All measurements of plant growth regulating effects were determined either by using a protoplast screening assay and/or by using a root growth assay and/or by applying the compounds pre-selected the before defined assay system under natural growth conditions in field trials. In all cases, untreated protoplasts, plants or plants parts, or seeds were taken as a control.

## B. Biological Examples

### Example 1. Plant Protoplast System

- 5 The present invention features a so called high throughput assay for a rapid screening of chemical compounds that modulate cell growth. The assay in general involves: a) plant protoplasts grown in liquid medium, b) a library of chemical compounds, and c) screening the protoplasts to identify the compounds which affect significantly the cell growth and development.

10

#### Protoplast preparation:

- Preferably the protoplasts were prepared from cell suspensions derived from maize callus. The protoplasts were obtained by enzymatic digestion of the cell aggregates in the suspension. The cells were digested for 3-6 hours at room temperature in a cellulase-pectolyase mix, Protoplasts were released by gentle shaking, filtered through a 45  $\mu$ m mesh and collected by centrifugation. After digestion, the protoplasts were washed several times to remove cell debris and enzyme residues and then re-suspended in culture medium. The protoplasts were plated in 50 - 100  $\mu$ l aliquots in microtiter wells at a density ranging from 100.000 - 2,000.000 protoplasts per ml, preferably at a concentration of 800.000 protoplasts/ml.

20

#### Screening assay:

- To identify chemical compounds that modulate the cell growth, maize protoplasts were incubated with a library of chemical compounds in 96-well microtiter plates. Following the incubation at 25°C for 1-14 days, preferably 7-10 days, the protein content was measured by Coomassie dye based colorimetric assays. The growth of the cells treated with the chemical compounds involved in the test was detected by comparison with untreated protoplasts.
- Treatment with a section of compounds derived from formula (I) show an increase of more than 50% over untreated control

30



## Example 2. Root growth assay

Plant roots are a highly proliferative tissue that allows an easy accessible, cheap and short term screening method for plant growth regulators. The results obtained can easily be transferred to the overall effects on a plant of plant growth regulators identified by such a system. By using this root assay one is enabled to determine the effect of a seed treatment to root growth and/ or germination and/ or changes in habitat of germinated plants in order to identify the possible use as a yield enhancer. Two seeds of wheat (*Triticum aestivum*, variety "TRISO") or 1 seed of maize (*Zea mays*, variety "LORENZO") per hole in a plastic tray which contains an architecture of 8 x 13 holes were placed on compost soil covered with sand. These seeds were treated with 100 µl/ hole, which creates an application volume of approx. 1200 l/ ha, of a compound solution at active ingredient rates equivalent to 100, 10 and 1 g a.i./ ha of each compound using an robotic application system (Lizzy Spray Robotics). Six replicates in a row of each compound and concentration were done. The outer rim of the above defined plastic tray was untreated to avoid false negative effects and the middle row (No. 7) was used as untreated control. The treated seeds were allowed to dry for approx. 4 hours and subsequently covered with sand and watered. The trays were stored in climate chambers with 14 hours lighting at a temperature of 24° C (± 2) at daytime and 16° C (± 2) at night and relative humidity (rH) of 60% and daily watered. Assessments were done 16 (± 2) days post treatment by counting the germinated plants and assessing the phytotoxicity symptoms and percentage. In addition, the roots were washed out and the shoots were cut directly above the seed and the wet roots were placed on dry paper towels for approximately 30 minutes and weighted afterwards. This procedure provides a similar grade of moisture to the roots so that a comparison of the weights is possible.

Table 3 shows the results of some of the compounds (Cpd) claimed to be effective in plant growth regulation concerning maize. The effects observed concerning Root Growth given in column 2 (Root Growth of "100" is set as the standard) are directed to concentrations that are equivalent to 100, 10, 1 g a.i./ha, each.

TABLE 3

Cpd	Maize (concentration g a.i./ha)		
	100	10	1
1.53	108	85	91
1.58	105	107	91
1.60	109	105	191
1.79	105	116	108

- 5 Table 4 shows the results of some of the compounds (Cpd) claimed to be effective in plant growth regulation concerning wheat. The effects observed concerning Root Growth given in column 2 (Root Growth of "100" is set as the standard) are directed to concentrations that are equivalent to 100, 10, 1 g a.i./ha, each.

TABLE 4

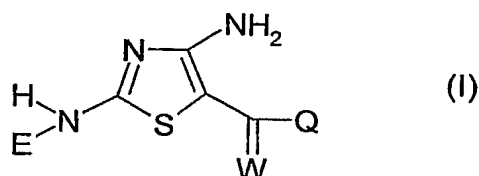
Cpd	Wheat (concentration g a.i./ha)		
	100	10	1
1.53	101	107	125
1.58	103	112	123
1.60	54	57	98
1.79	73	88	88
1.105	123	99	72
1.106	90	99	145
1.108	131	95	78
1.117	125	126	111
1.118	113	122	95
1.139	120	66	130

## Claims

BCS 03-1031

1. Use of a compound of formula (I) or an agriculturally acceptable salt thereof for plant growth regulation

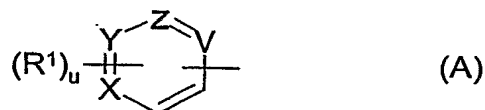
5



wherein:

E is (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>3</sub>-C<sub>6</sub>)alkynyl, (C<sub>1</sub>-C<sub>6</sub>)alkoxy-(C<sub>1</sub>-C<sub>6</sub>)alkyl, [(C<sub>1</sub>-C<sub>6</sub>)alkoxy]carbonyl-(C<sub>1</sub>-C<sub>6</sub>)alkyl, [(C<sub>1</sub>-C<sub>6</sub>)alkyl]carbonyloxy-(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl-(C<sub>1</sub>-C<sub>6</sub>)alkyl, furfuryl, tetrahydrofurfuryl or isoxazoly which last mentioned group is unsubstituted or substituted with one or two (C<sub>1</sub>-C<sub>6</sub>)alkyl radicals; or is a group of formula (A):

10



15

in which X, Y, Z and V are each independently C or N, with the proviso that at least two of X, Y, Z and V are C;

the linking bond of (A) is attached to a ring carbon atom;

20

(R<sup>1</sup>)<sub>u</sub> are u substituents of R<sup>1</sup> which may be same or different, each R<sup>1</sup> is linked to a ring carbon atom and is H, R<sup>2</sup>, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl-(C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl-(C<sub>1</sub>-C<sub>6</sub>)alkoxy, [(C<sub>3</sub>-C<sub>8</sub>)cycloalkyl]carbonyl, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyloxy, (C<sub>3</sub>-C<sub>8</sub>)cycloalkyl-S(O)<sub>m</sub>, (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl or (C<sub>2</sub>-C<sub>6</sub>)alkynyl where each of the last 3 mentioned radicals is unsubstituted or substituted by one or more R<sup>2</sup> radicals;

25

or aryl, heterocyclyl, aryl-(C<sub>1</sub>-C<sub>6</sub>)alkyl, heterocyclyl-(C<sub>1</sub>-C<sub>6</sub>)alkyl, aryl-(C<sub>1</sub>-C<sub>6</sub>)alkoxy, heterocyclyl-(C<sub>1</sub>-C<sub>6</sub>)alkoxy, aryl-carbonyl, heterocyclyl-carbonyl, aryloxy, heterocycliloxy, aryl-S(O)<sub>n</sub> or heterocyclyl-S(O)<sub>p</sub>, where the aryl or

heterocyclyl portion of the last 12 mentioned radicals is unsubstituted or substituted by one to three radicals selected from the group consisting of  $R^2$ ,  $(C_1-C_6)$ alkyl,  $(C_2-C_6)$ alkenyl and  $(C_2-C_6)$ alkynyl, where each of the last 3 mentioned radicals is unsubstituted or substituted by one or two  $R^2$  radicals;

5 or (A) is fused to a 1,3-dioxolanyl or 1,4-dioxanyl ring where each of the last two mentioned rings is unsubstituted or substituted by one or more radicals selected from the group consisting of halogen,  $(C_1-C_6)$ alkyl,  $(C_1-C_6)$ alkoxy and OH;

each  $R^2$  indepently form other  $R^2$  radicals is hydroxy, halogen, cyano, nitro,

10  $NR^3R^4$ ,  $CONR^3R^4$ ,  $ONR^3R^4$ ,  $OCH_2CONR^3R^4$ ,  $(C_1-C_6)$ alkoxy,  $(C_1-C_6)$ haloalkoxy,  $CO_2R^3$ ,  $COR^3$ ,  $NHCOR^3$ ,  $NHCO_2R^3$ ,  $S(O)_qR^5$ ,  $SO_2NH_2$  or  $R^6$ ;  $R^3$  is hydrogen,  $(C_1-C_6)$ -alkyl or  $CH_2R^6$ ;

$R^4$  is hydrogen or  $(C_1-C_6)$ -alkyl; or  $R^3$  and  $R^4$  together with the nitrogen atom to which they are attached form a 3 to 8 membered cyclic ring optionally

15 containing one or two further hetero atoms selected from oxygen, sulfur and nitrogen;

$R^5$  is  $(C_1-C_6)$ alkyl or  $(C_1-C_6)$ haloalkyl;

W is O or  $N-OR^7$ ;

$R^6$  is phenyl unsubstituted or substituted by one or more radicals selected

20 from the group consisting of halogen,  $(C_1-C_6)$ alkyl,  $(C_1-C_6)$ haloalkyl and  $(C_1-C_6)$ alkoxy;

$R^7$  is hydrogen,  $(C_1-C_6)$ alkyl or aryl- $(C_1-C_6)$ alkyl;

Q is  $(C_3-C_8)$ cycloalkyl,  $(C_3-C_8)$ cycloalkyl- $(C_1-C_6)$ alkyl, where the last 2 mentioned radicals are unsubstituted or substituted in the cycloalkyl by  $(C_1-C_4)$ alkyl,  $(C_1-C_4)$ alkoxy and halogen,  $(C_1-C_6)$ alkyl,  $(C_2-C_6)$ alkenyl or  $(C_2-C_6)$ alkynyl, where each of the last 3 mentioned radicals is unsubstituted or

25 substituted by one or two  $R^2$  radicals; or

aryl, heterocyclyl, aryl- $(C_1-C_6)$ alkyl or heterocyclyl- $(C_1-C_6)$ alkyl, where the aryl or heterocyclyl portion of the last 4 mentioned radicals is unsubstituted or

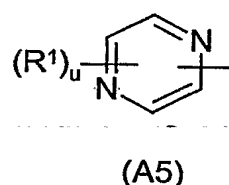
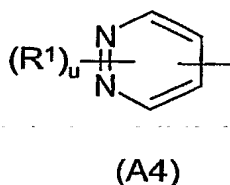
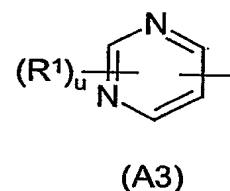
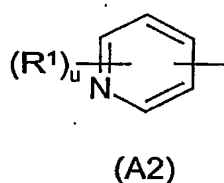
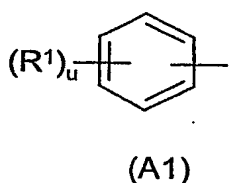
30 substituted by:

i) one to three radicals selected from the group consisting of  $R^2$ ,  $(C_1-C_6)$ alkyl,  $(C_2-C_6)$ alkenyl and  $(C_2-C_6)$ alkynyl, where each of the last 3

mentioned radicals is unsubstituted or substituted by one or two  $R^2$  radicals;  
or

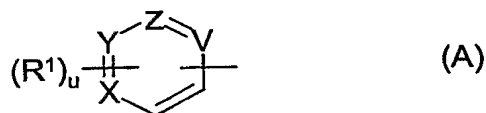
- ii)  $(C_3-C_8)$ cycloalkyl,  $(C_3-C_8)$ cycloalkyl- $(C_1-C_6)$ alkyl,  $(C_3-C_8)$ cycloalkyl- $(C_1-C_6)$ alkoxy,  $[(C_3-C_8)$ cycloalkyl]carbonyl,  $(C_3-C_8)$ cycloalkyloxy,  $(C_3-C_8)$ cycloalkyl-S(O)<sub>r</sub>, aryl, heterocyclyl, aryl- $(C_1-C_6)$ alkyl, heterocyclyl- $(C_1-C_6)$ alkyl, aryl- $(C_1-C_6)$ alkoxy, heterocyclyl- $(C_1-C_6)$ alkoxy, aryl-carbonyl, heterocyclyl-carbonyl, aryloxy,  $(C_3-C_8)$ -heterocyclklyoxy, aryl-S(O)<sub>s</sub> or heterocyclyl-S(O)<sub>t</sub>, which last 12 mentioned radicals is unsubstituted or substituted by one or two radicals selected from the group consisting of  $(C_1-C_6)$ alkyl,  $(C_2-C_6)$ alkenyl,  $(C_2-C_6)$ alkynyl and  $R^2$ ;  
m, n, p, q, r, s and t are each independently 0, 1 or 2;  
u is the number of ring carbon atoms in formula (A) minus 1;  
and each heterocyclyl in the above-mentioned radicals is independently a heterocyclic radical having 3 to 7 ring atoms and 1, 2 or 3 hetero atoms in the ring selected from the group consisting of N, O and S.

2. The use of a compound as defined in claim 1, in which (A) of formula (I) is a formula (A1), (A2), (A3), (A4) or (A5):



and wherein  $R^1$  and u are as defined in claim 1.

3. The use of a compound as defined in claim 1, in which E is  $(C_1-C_6)$ alkyl,  $(C_1-C_6)$ alkoxy- $(C_1-C_6)$ alkyl,  $[(C_1-C_6)$ alkoxy]carbonyl- $(C_1-C_6)$ alkyl,  $(C_3-C_8)$ cycloalkyl- $(C_1-C_6)$ alkyl or a group (A):

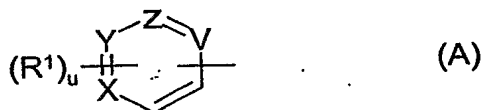


X, Y, Z and V are each C;

each R<sup>1</sup> which may be the same or different is H, hydroxy, halogen, cyano, nitro, NR<sup>3</sup>R<sup>4</sup>, CONR<sup>3</sup>R<sup>4</sup>, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, CO<sub>2</sub>R<sup>3</sup>, COR<sup>3</sup>, NHCOR<sup>3</sup>, S(O)<sub>q</sub>R<sup>5</sup>, SO<sub>2</sub>NH<sub>2</sub>, (C<sub>1</sub>-C<sub>3</sub>)alkyl or (C<sub>1</sub>-C<sub>3</sub>)haloalkyl, wherein R<sup>3</sup> and R<sup>4</sup> are each independently hydrogen or (C<sub>1</sub>-C<sub>3</sub>)-alkyl, and R<sup>5</sup> is (C<sub>1</sub>-C<sub>3</sub>)alkyl or (C<sub>1</sub>-C<sub>3</sub>)haloalkyl;

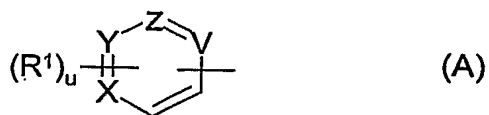
or phenyl or pyridyl, which last 2 mentioned radicals are unsubstituted or substituted by one to three radicals selected from the group consisting of halogen, (C<sub>1</sub>-C<sub>6</sub>)alkyl and (C<sub>1</sub>-C<sub>3</sub>)haloalkyl; and u is 5.

4. The use of a compound as defined in claim 1, in which E is (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy-(C<sub>1</sub>-C<sub>3</sub>)alkyl, [(C<sub>1</sub>-C<sub>3</sub>)alkoxy]carbonyl-(C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl-(C<sub>1</sub>-C<sub>3</sub>)alkyl or a group of formula (A):



X, Y and Z are all C; V is C or N; R<sup>1</sup> is H or halogen; and u is 4 or 5.

5. The use of a compound as defined in claim 1, in which E is (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy-(C<sub>1</sub>-C<sub>3</sub>)alkyl, [(C<sub>1</sub>-C<sub>3</sub>)alkoxy]carbonyl-(C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl-(C<sub>1</sub>-C<sub>3</sub>)alkyl or a group (A):



X, Y, Z and V are all C;

W is O;

5 R<sup>1</sup> is H or halogen;

Q is cyclopropyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, phenyl, naphthyl, pyridinyl, tetrahydropyridinyl, thienyl or benzo[b]thienyl, which last 6 mentioned radicals are unsubstituted or substituted by one to three radicals selected from the group consisting of halogen, (C<sub>1</sub>-C<sub>3</sub>)alkyl, OH, NO<sub>2</sub>, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, (C<sub>1</sub>-C<sub>3</sub>)haloalkoxy, phenyl and benzyloxy; and

10 u is 5.

6. A composition for plant growth regulation, which comprises one or more compounds of formula (I) as defined in anyone of claims 1 to 5 or an agriculturally acceptable salt thereof, carriers and/or surfactants useful for plant protection formulations.

15

7. The composition as claimed in claim 6, which comprises a further active compound selected from the group consisting of acaricides, fungicides, herbicides, insecticides, nematocides or plant growth regulating substances not identical to compounds defined by formula (I) of claim 1.

20

8. The use of a composition as claimed in anyone of claims 6 to 7 for plant growth regulation, in which the plant is a monocotyledoneous or dicotyledoneous crop plant.

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9. The use as claimed in claim 8, wherein the plant is selected from the group consisting of wheat, barley, rye, tritcale, rice, maize, sugar beet, cotton, or soybeans.

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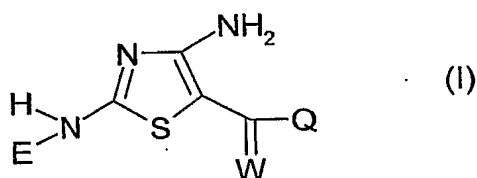
10. A method for growth regulation in crop plants, which comprises applying an effective amount of a compound of formula (I) as defined in claims 1 to 5 to the site where the action is desired said method comprising applying to plants, to seeds from which they grow or to the locus in which they grow, a non-phytotoxic, effective plant growth regulating amount of one or more compounds of formula (I).
11. A method as claimed in claim 10 that results into a yield increase of at least 10% concerning the plants to which it is applied.



Abstract

BCS 03-1031

The present invention relates to a new class of plant growth regulators. In particular,  
the invention relates to 2,4-diamino-5-substituted-thiazole derivatives of general  
5 formula (I)



and a method for treatment of plants with such compounds in order to induce growth  
10 regulating responses.

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